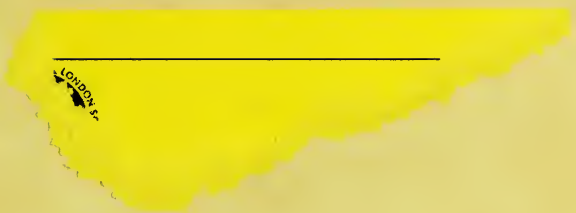

# MALARIAL FEVERS
# AND
# MALARIAL PARASITES
# IN INDIA.

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BY

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*WITH THIRTY-SIX ILLUSTRATIONS AND TWENTY-FIVE CHARTS.*

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OCTOBER 1901.

Printed at the Central Jail Press, Nagpur.

To

The Hon'ble Mr. A. H. L. Fraser, C. S. I.,

Chief Commissioner, Central Provinces, India,

WHO HAS TAKEN MUCH INTEREST IN THE INVESTIGATIONS,

HEREIN RECORDED,

THIS HUMBLE CONTRIBUTION TO THE STUDY OF MALARIA IS

BY PERMISSION

MOST RESPECTFULLY DEDICATED.

# PREFACE.

SO much has been written on the subject of Malaria in the past few years one feels that it is necessary to make some apology for adding to the already very extensive literature on the subject. Celli in his very valuable book on Malaria gives a good account of Malarial fevers in Italy. Manson, who has probably done more than any other man to stimulate enquirers to make investigations into the nature and causation of Malarial fevers, has given a very excellent account of these fevers in his book on Tropical Diseases. Ross, Christophers, Stephens and others have described the Malarial fevers of the West Coast of Africa, but no one has, as far as I am aware, given a complete account of the Malarial fevers of India.

It is not claimed for what is written here that it is a complete account of the Malarial fevers of India. It is merely a record of a series of observations that have been made during the past 12 months. The observations were made in the Nagpur Central Jail, where five high power microscopes have been in regular use for the greater part of the year. A number of Burmese prisoners were trained to use the microscopes and they very soon became expert in detecting and distinguishing the various kinds of parasites. Others were trained to take temperatures so that the record of parasites could easily be compared with the record of temperatures. One Burman, Ko Tha Aung, took an exceptionally keen interest in the subject, and carefully studied most of the literature that has appeared in Medical and non-Medical Journals on Malaria in recent years. Nga Weh Kyi, Nga Kyi, Nga Pe Gyi, Nga Hman, and Goverdhan have also given most valuable assistance.

Should the observations which are here recorded be considered by the Government of any value, I hope that something may be done to lessen the term of imprisonment of the men whose names have been mentioned, for without their assistance, and if they had not taken the keenest interest in the work, it would not have been possible to make these investigations.

I should like to express my thanks to Colonel Quayle, I. M. S., and Dr. Agnes Henderson for very kindly lending us their excellent microscopes and for assisting in making the observations.

There are many parts of this small book which I should like to rewrite, but as the time at my disposal for such work at present is very limited, I think it is better to publish the observations as they were originally written, in the hope that they may be of some service to the many men who are now engaged in the great campaign against the Malarial parasites.

A. BUCHANAN, Major I. M. S.

*October 1901.*

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# MALARIAL PARASITES AND FEVERS IN INDIA.

## CHAPTER I.

### FORMS OF PARASITES.

In this chapter a short description of the various kinds of parasites that are seen in the blood of malarial cases and a short explanation of the terms that are employed will be given. There is only one really good way to learn what the parasites are like, and that is, to see the parasites themselves. If a whole book were written giving a description of a cow, and another book were written giving a description of a buffalo, and a person after having thoroughly studied these two books were for the first time to see a cow, and a buffalo, he would perhaps have some difficulty in deciding which is the cow and which is the buffalo. If he saw the animals themselves and if the differences were pointed out he would have no difficulty afterwards in distinguishing the cow from the buffalo. In the same way, no amount of book study can convey such a knowledge of the parasites as might be gained from a few hours' demonstration of the real parasites. Some assistance may however be given by illustrations, but even the best illustrations must be very different from the real parasite, especially as a great characteristic of many of the forms of parasite is their movement and the illustration cannot convey any accurate idea of this movement.

*(1) The young unpigmented parasite.*—When the young parasites first enter the red blood corpuscles they are without pigment. They occupy a small portion of the red blood corpuscle, and they may be moving or quiescent. If they are moving it is easy to recognise them. The movement is what is called amœboid, *i. e* the movement is merely a change of shape, not a change of position. The following illustrations will give an idea of the various shapes that a parasite may assume within a few minutes. The parasite is represented inside a red blood corpuscle, and it should be explained that for facility in illustration the size of the parasite and red blood corpuscle have been made larger than they are usually seen under a high power microscope.


Drawn at one minute interval: Malignant Tertian.

*(2) The young pigmented parasite.*—In a few hours pigment appears inside the young parasite. The size and rapidity of movement of the pigment varies according to the kind of parasite. In one kind it is coarse and its movement is slow. In another kind it is fine and moves quickly. In another kind it is small in amount, but these differences will be explained fully later on. The following illustrations show the appearance of some young forms with pigment :—

(3) As the parasites grow larger the amount of pigment increases. Some parasites fill the whole red blood corpuscle.

Quartan parasite.

B. Tertian parasite.

Some while seen in the peripheral blood only invade a small part of it.

M. Tertian parasites.

*(4) Rosettes.*—When the parasite has attained a certain stage, it becomes divided into segments, and assumes the form to which the name Rosette or a Daisy form has been applied.

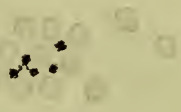
Then the segments are still further separated and each segment forms a spore, or young parasite. The breaking up of the Rosettes corresponds in time with a fresh onset of fever, and if the blood is examined when the patient is shivering rosettes may be seen. But the rosettes are rarely seen in Malignant Tertian while they can be very easily seen in Quartan. The growth of the Rosette can be watched under the microscope.

The pigment is at first scattered all through the parasite or chiefly at the circumference. The pigment begins to collect into the centre and the division into segments becomes apparent. In each segment a nucleus is perhaps seen.

Quartan rosettes.

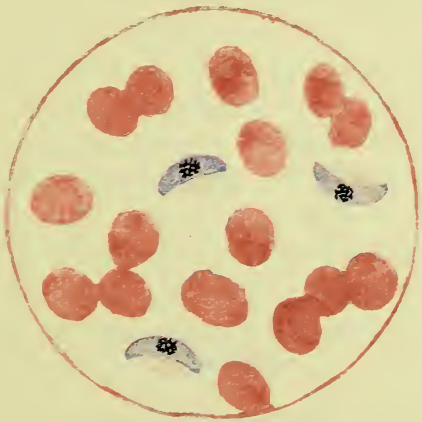
The segments are still further separated and each segment forms a spore.

The rosette breaks up and the spores separate :—



*(5) Crescents.*—The next illustration gives a very fair idea of the appearance of a crescent or as it is sometimes called the crescent body. It is very easily recognised. It is not found in the two kinds of fever which belong to the Benign group, but is found in the Malignant group. The name Crescent is not altogether a satisfactory one, for the crescent body is not always of a crescentic shape. It is sometimes spindle-shaped, sometimes round, sometimes oval, but most frequently it is of a crescent shape.

On the concave side of the crescents we sometimes see a fine line enclosing what we may for want of a better name call the" belly." The belly part is the remains of the red blood corpuscle. It is perfectly clear, and only the very fine line which marks the boundary of it can be seen in unstained specimens. In stained specimens, however, the belly part is coloured red with eosine showing that it is part of the original red blood corpuscle.



(6) *Flagella and the Flagellar bodies.*—The parasites have two methods of reproduction, one the asexual and the other the sexual method. The formation of and the breaking up of the Rosette is the asexual method of reproduction. The flagella take part in the sexual method of reproduction. In the Malignant forms the flagella come from the crescents. In the Benign forms the flagella come from what look like the ordinary full grown parasites. Flagella are seldom seen in the Benign fevers, they are frequently seen in the Malignant fevers.

The forms of parasite will be described more fully in subsequent chapters. What has been written here is intended to give to anyone who has not seen the parasites a rough idea of the nature of the parasites and of the names which are applied to the various forms of parasites.

## CHAPTER II.

### CLASSIFICATION OF PARASITES.

Manson describes 5 forms of Malarial parasites, *viz*, Quartan, Benign Tertian, Malignant Tertian, Unpigmented Quotidian, and Pigmented Quotidian. Celli also describes the same forms. Koch in a lecture delivered on the 15th November last at Berlin says " it was also ascertained that the apparently different Italian forms of malaria are really one, and that apart from Quartan and Tertian which occur among ourselves there really is only one form of malaria, namely 'tropical malaria.' " In the same lecture Koch also states "Germany has two kinds of malaria, Italy three, and a fourth kind tropical malaria, is found in the Tropics." Koch in this lecture does not say what are the three kinds that are found in Italy nor what is the nature of the malaria which he calls Tropical.

During the past two months, that is from the middle of December till the middle of February, we have seen four distinct kinds of parasites and four distinct kinds of fever corresponding to these four parasites. Parasites were not found in every case, but they were found in nearly all of those who had high temperatures. It is very remarkable that the kinds of malaria found here tally almost exactly with those found in Italy. We have not however found any cases of what has been called the Unpigmented Quotidian. The following are the varieties which have been met with here :—

| | | |
|---|---|---|
| Quartan | ... | 9 |
| Benign Tertian | ... | 11 |
| Malignant Tertian | ... | 46 |
| Pigmented Quotidian | ... | 2 |

By the microscope it is sometimes extremely easy to distinguish the various forms of parasite, but in cases where there are only a few parasites to be seen there may be some difficulty. The best way to learn the distinguishing characters is to consider—

*1st.*—What points are common to all.

*2nd.*—In what respects do the Benign group resemble each other, and differ from the Malignant group.

*3rd.*—What are the differences between the two parasites of the Benign group, and

*4th.*—What are the differences between the two of the Malignant group?.

The points that are common to all kinds are :—

(1) All are amœboid and grow inside the red blood corpuscles.

(2) All eat up the red blood corpuscles destroying their colouring matter.

(3) All form black pigment.

(4) All are colourless (excepting the pigment.)

(5) All stain with methylene blue.

(6) All have a definite period of growth: Quartans 72 hours, Tertians 48 hours, and Quotidians 24 hours.

(7) All have two methods of reproduction—one the asexual and the other the sexual.

(8) All form "rosettes."

(9) All give out "flagella."

The Benign Tertian and Quartan have many points in common and the Malignant Tertian and the Quotidian have also many points of resemblance. The two former have several common points of difference from the two latter, and the two latter have several common points of difference from the two former. The two former, called mild malaria, (Benign) by Celli, differ from the two latter, which are called severe malaria (Malignant) by the same writer.

| Quartan and Benign Tertian | Malignant Tertian and Quotidian. |
|---|---|
| Invade whole red blood corpuscles. | Invade only $\frac{1}{4}$ of red blood corpuscle while they are seen in the peripheral blood. |
| Seen in peripheral blood throughout whole cycle. | The young forms are seen in the peripheral blood, and then they disappear from it for some days until they have become transformed into crescents. |
| Do not form crescents. | |
| Rosette forms seen frequently. | Seldom. |

Thus there are four main points in which the Quartan and Benign Tertian resemble each other, and in which these two differ from the Malignant parasites. The two former invade the whole red blood corpuscle and for this reason it is very easy to find them. The latter two invade only about one-fourth of the red blood corpuscle while they are seen in the peripheral blood and then they retire or conceal themselves (in the spleen or in the marrow of the bones, but this we have not investigated here) until they have become converted into crescents. This temporary retirement of the parasites from active life in the peripheral blood is a

very remarkable phenomenon. It would seem almost as if there were a barrier through which each corpuscle has to pass and that admission to those carrying the crescent forming parasites is strictly forbidden. If the red blood corpuscles which carry these parasites were enlarged, then we might be able to explain this curious phenomenon, but they are not larger, and there is no such prohibition exercised in the case of the big swollen red blood corpuscles in which the Benign Tertian parasites have located themselves.

The two former differ from the two latter also as regards their Rosette forms, which are seen often in the case of the former and seldom in the case of the latter.

It is a curious thing that some of the parasites in the two latter kinds are converted into crescents and some are converted into rosettes—the former a step in the sexual method of reproduction, the latter a step in the asexual method of reproduction. What determines the form into which any particular parasite will develop we cannot say nor have we seen any explanation offered.

The two members of the Benign group differ from each other in the following points :—

| Quartan. | Benign Tertian. |
|---|---|
| The invaded red blood corpuscle not enlarged. | Invaded red blood corpuscle enlarged. |
| The part of red blood corpuscle which has not been eaten still retains the ordinary colour of the red blood corpuscle. | The red blood corpuscle loses its colour and becomes clear. |
| The pigment is in large granules | The pigment is in rods. |
| The pigment moves slowly. | The pigment moves rapidly. |
| The Rosette has 8 to 10 parts. | The Rosette has about 20 parts. |

It should be explained that the above differential points do not always hold good; for instance, the pigment in a Quartan may be moving very actively when flagella are about to be thrown out, or the pigment of a Benign Tertian may not appear to be in rods when the parasite is young. There are many other minor points of difference but these will be referred to later.

The Malignant Tertian and the Quotidian belong to the Malignant group, and the chief characteristic of this group is that they form crescents. The differences between these two are slight: the young Quotidians are more active, and there is a difference in the number of parts which are seen in the Rosettes, but the differences in the Rosettes will be explained later. There are two other points of difference which we believe are useful in distinguishing the Quotidians from the Malignant Tertians, but it should be explained that these two points are not mentioned by any authors we have read, and we have not had a sufficient number of cases of Quotidian to justify us in saying if these points of distinction always hold good. We believe that the Quotidian crescents are larger and the Quotidian pigment is in longer rods than that of the Malignant Tertian.

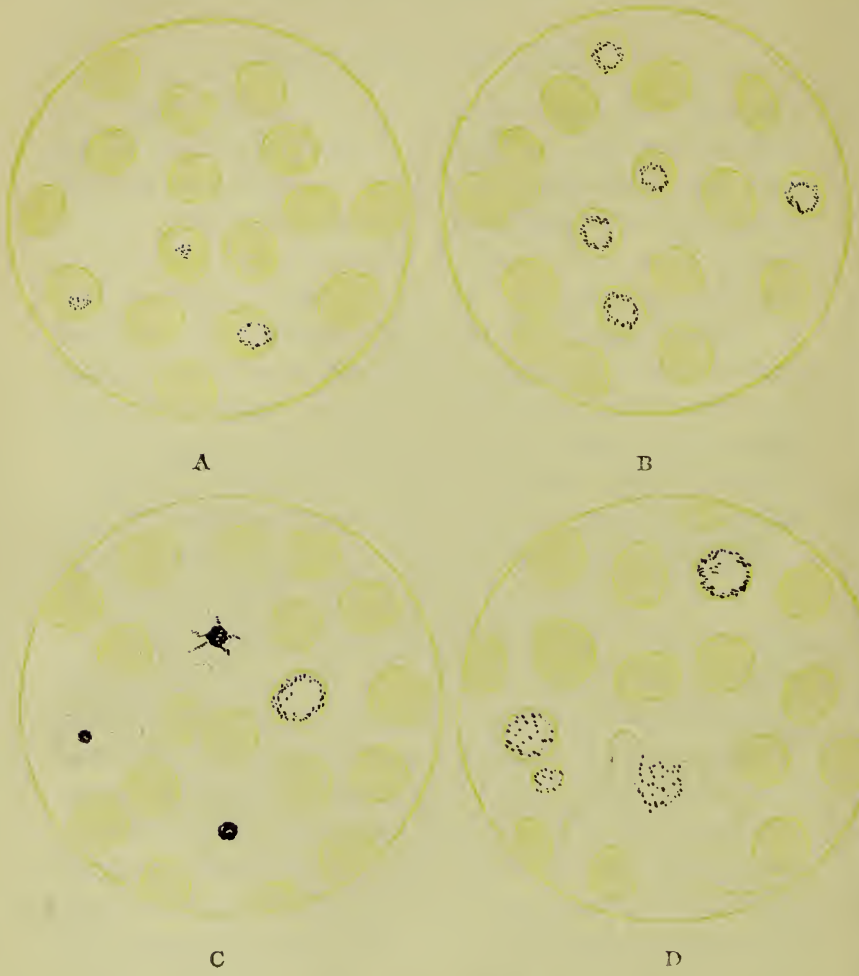
## CHAPTER III.

### QUARTAN FEVER.

In the Introductory Lecture which Crombie gave at the Indian Medical Congress in Calcutta in 1894 he said that Quartan fever was very rare and that "I had only to treat one case of Quartan in the whole of my 22 years' service in India." We were also of opinion that Quartan fever was very rare, and although we had been watching specially for Quartan cases for some years it was very rare to find any. During the past two months, while the observations which are here recorded were being made, we have had 9 cases of Quartan fever in Hospital, and the question arises how is it that we have seen so many cases of Quartan in this short space of time, and that for years before we had not been able to discover a case?

The reasons are probably these. In the first place Quartan yields to quinine very readily, and a patient suffering from Quartan may have been detained for a day in Hospital, and if treated with quinine his fever would probably stop. Or we may have been misled by the appearance of the charts, for if temperatures are taken only twice daily, the attack may not have come on at the time the temperature was taken. We have recently taken the temperatures every two hours, night and day, and oftener during the time that the paroxysms were occurring, and the charts have been prepared from the two hour records. For instance, it has frequently happened that a Quartan paroxysm has come on at 8 o'clock at night and the temperature may have been normal at 5 o'clock in the afternoon, so that a chart prepared from the 5 o'clock record would be quite misleading.

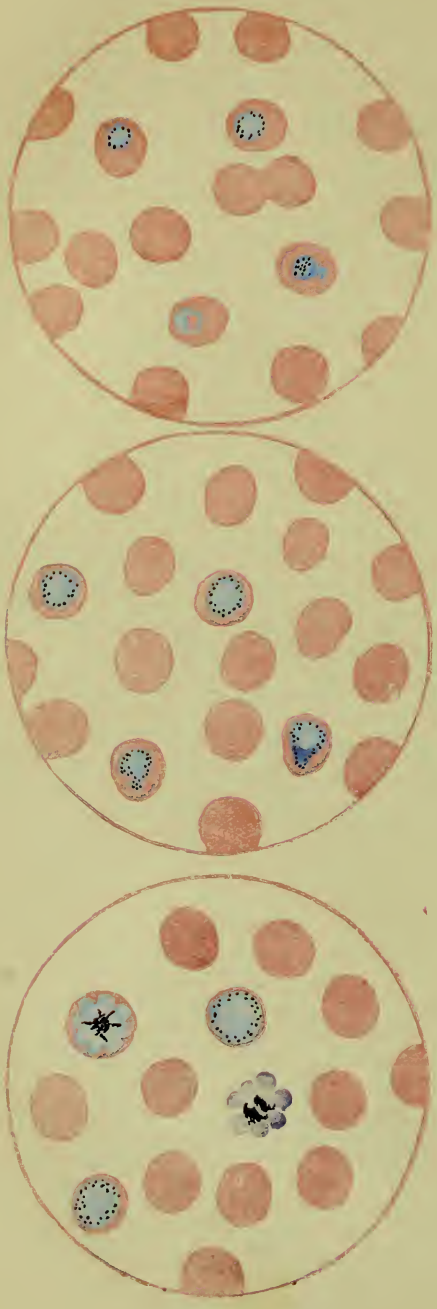
## QUARTAN PARASITES.



A. 1st day: Young parasites; some without and some with pigment.
B. 2nd day.
C. 3rd day when fever is coming on: forming Rosettes:
D. One full grown: flagella body (rarely seen)

Opposite page 13.

QUARTAN PARASITES STAINED.



A. 1st day: young parasites, some with pigment and some without pigment.

B. 2nd day: pigmented middle age parasites.

C. 3rd day: full grown parasites and rosettes forming when fever comes on.

Further, in Quartan fevers it sometimes happens that there is a rise of temperature every day and in such cases the chart made from a twice a day record may not show the least indication of a Quartan fever.

Besides, it is only recently that we have made a systematic examination of the blood of every case admitted for fever, and as we have several men working daily and throughout the whole day it is almost impossible for Quartan parasites to pass undetected.

Then again we have had some cases of Quartan combined with other kinds of fever as Malignant Tertian, and in these cases the Quartan appearance of fever is not seen at least in the early days of the patient's residence in Hospital. Quartan fever may therefore be more common than we have hitherto been inclined to believe.

*Parasites.*—In the tables given at pages 9 and 10 we have already given the points in which the Quartans resemble the Benign Tertians and the points of difference between these two parasites. The illustrations give a very fair idea of the appearance of Quartan parasites. There are two sets of illustrations—one showing the unstained parasites, the other showing the parasites stained with methylene blue and the corpuscles with eosine.

*Unstained Quartans.*—The parasite is very easily seen. It seems to be an irregular clear space inside the corpuscle, with coarse granules of pigment. The pigment is generally at the circumference of the parasite and is not scattered through the parasite as it is in Benign Tertian. The parasite is more or less circular with an irregular outline, and we never find

three or four long arms extending into the corpuscle as we do in Benign Tertian. The pigment is slow moving, so slow that the movement can scarcely be seen while we are watching it, but if a sketch be made and another made a few minutes afterwards it will then be seen that the pigment has altered its position. In parasites which are going to give out flagella we however will find that the pigment is moving very actively (D).

From an examination of a specimen of blood drawn from a Quartan case it is generally possible to tell not only the kind of fever but the age of the parasite, and we can tell whether fever will come on that day, on the next day, or the next day but one. The one-day old parasite occupies about one-third of the corpuscle (A), the two-day old parasite occupies about two-thirds of the corpuscle (B), and the three-day old parasite fills or almost entirely fills the corpuscle (C). Rosettes will be seen shortly before the paroxysm of fever comes on, but the best time to get them is just as the shivering stage begins (C).

It is only a few years since a Medical man of high standing in India wrote in regard to these parasites, that they were not the cause of the malarial fevers; but anyone who has watched a case of Quartan fever has seen how regularly the Rosettes appear at the cold stage, how regularly the parasites grow, how they disappear when the fever stops, and how constant is their appearance in every Quartan case, cannot fail to be convinced that these parasites are the cause of the fever.

The Quartan is remarkable for its regularity and for its persistence, and for these reasons it offers the best opportunity of testing the value of drugs. We have tested the effects of the two medicines which are most frequently given for Malarial fevers. The effect of quinine is marvellous. One dose of xx grains of quinine has not yet failed to stop the paroxysms of fever for a time at least, but arsenic, if it has any effect at all, would seem to act as a good tonic for the parasite. The effect of the medicines is judged by the examination of the blood as well as by the effect on the temperature.

Crombie in the Presidential address referred to above said "there are many practitioners in this country who, from timidity or wrong teaching or some other cause, have no knowledge of, and I fear no belief in the power of quinine as an antidote for malarial poisoning." If all cases with fever, whether of malarial origin or otherwise, are indiscriminately treated with quinine it can be easily understood how some of the fevers may yield to quinine and some may not, and if the medical man happens to be giving to cases that are not really malarious, large doses of quinine it will easily be understood how he may come to lose faith in the efficacy of quinine. Then again the different kinds of parasite may be affected to a different extent by quinine. It would be well therefore to put aside all ideas of treatment that have been derived from the administration of quinine, not only to malarial and non-malarial cases of fever indiscriminately, but to cases of malarial fevers which owe their origin to different parasites. The only scientific method is first to be certain that the cause of the fever

is malaria, and second to make certain what particular form of malarial parasite we are dealing with, then give the medicine and watch its effect, not only on the temperature but also on the parasite.

Working on these lines there is only one conclusion that can be arrived at from an examination of the cases that will be given here, and that is that quinine has a marvellous effect on the Quartan parasites. One dose of xx grains stopped the paroxysms in every case, and the parasites ceased to grow. A few were seen on the first day after the quinine was given, and on the following day they had disappeared. One dose of quinine is not however sufficient to kill them completely, although it stops the paroxysms of fever for some days for the fever may return and the parasites may after a week or two be again found in the blood.

In the same address, Crombie refers to the widespread belief:—

> " among medical men as well as among the laity, that quinine cannot be safely or efficiently administered except during the period of apyrexia, or at least in remittent fever its administration must be delayed till a remission has occurred such as to bring the temperature down to some point below 100° F. All the best authorities advocate a very opposite plan of treatment and I am glad to have this public opportunity of recording an emphatic dissent from the popular belief and practice. Careful observations have shown that quinine is most efficient against the malarial organism in the early period of its growth while it is still unpigmented or only collecting pigment at its periphery, *i. e.* in Quotidian* ague during the pyrexia and the crisis."

---

* NOTE.—Crombie had not apparently noticed that there are two kinds of Tertian, and the Quotidian referred to may probably include one form of Tertian, viz. the Malignant Tertian. In his Lecture only three kinds of fever are mentioned,—the Quartan, Tertian, and Quotidian.

> " When the amœba ceases to grow and begins to prepare for segmentation and sporulation, that is just before the rigor and new accession of fever, quinine has little or no effect on it."

We have given quinine in these when the spores, *i. e.* young parasites were entering the red blood corpuscles, when they were one day old, when they were two days' old, and when the parasites were full grown just ready for sporulation. The effect in all was the same. The parasites were killed and they disappeared entirely or almost entirely from the blood.

In our books on Materia Medica we find quinine classed among the medicines that are called "antiperiodics." This term was used before the nature of the action of quinine on the malarial parasite was understood. The quinine seems to act as a direct poison to the malarial parasites, and as our knowledge advances we may hope to see the old term antiperiodic fall into disuse, and another term, which more clearly indicates the nature of the action of such medicines, introduced in its stead.

Natives use a root called "*atthis*" in Malarial fevers and we are trying it in some Quartan cases, but its effect is not as good as quinine.

# CHAPTER IV.

## CHARTS OF QUARTAN.

Eight temperature charts will be reproduced. The first of these will illustrate what may be called "*severe*" Quartan or cases of Quartan in which there is fever every day. The Quartan charts have been divided into three-day periods, and it will be seen that on the first day of each period the temperature is high, on the second day it is above normal but not as high as on the first day, and on the third day it is below or near the normal line.

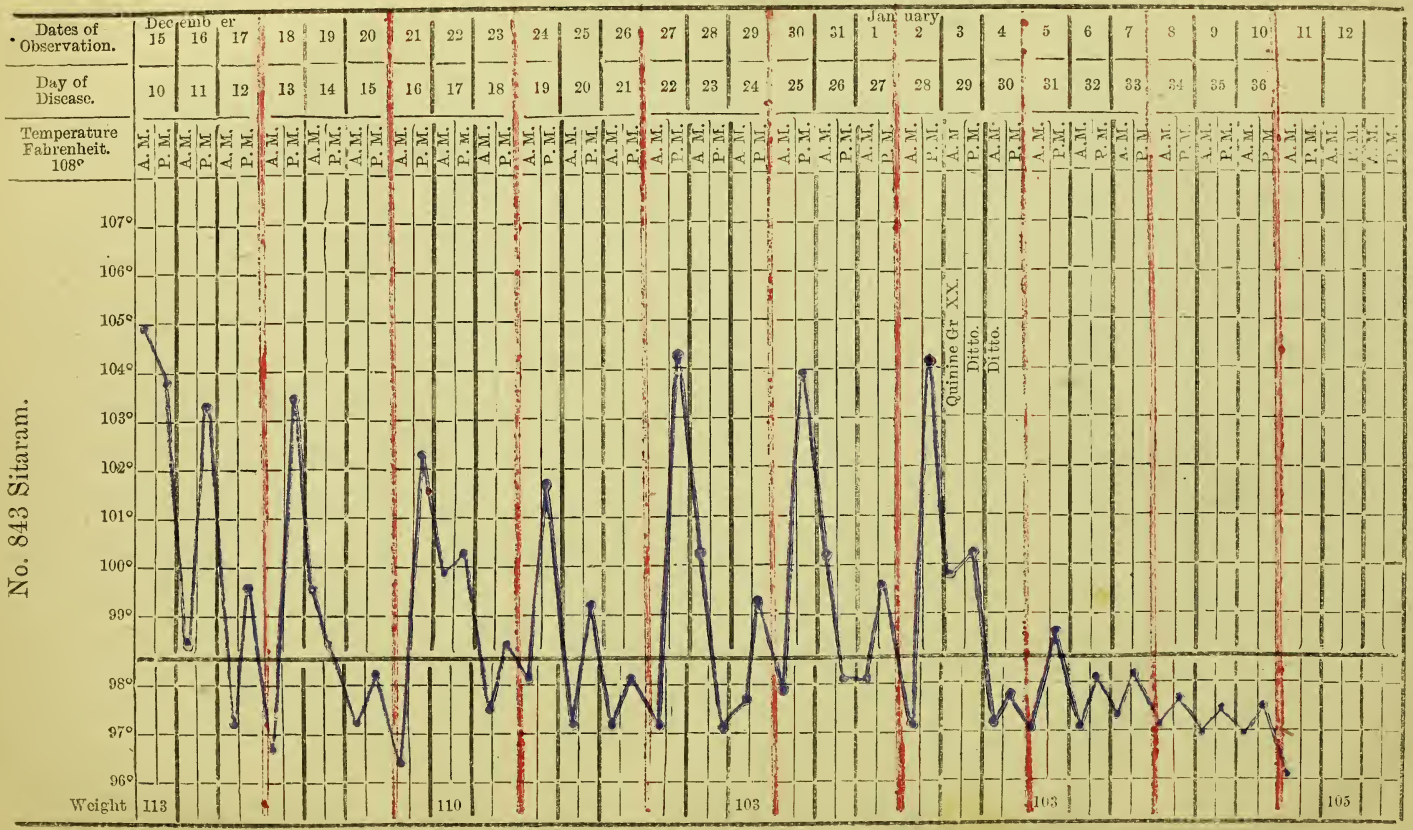
The next group might be called *clear* Quartans, *i. e.* with fever on one day and no fever on the two following days.

The next group show Quartan combined with other malarial fevers.

There are two other interesting charts which show Quartans combined with other diseases, one combined with Enteric Fever and the other Quartan combined with Pneumonia, but these two charts will not be given.

*Case I—Sitaram.* This chart shows the high temperature on the first day, a lower temperature on the second, and a nearly normal temperature on the third. This chart has been made out from the record of temperatures which have been taken every two hours. This case illustrates the tendency for Quartan paroxysms to recur if the case is not treated with

# QUARTAN CHART.



quinine. It also illustrates the good effect of quinine. In this case three doses of xx grains each were given on three successive days and the parasites disappeared and have not returned. Rosettes were found in large numbers and it was noticed that the best time to get large numbers of them was just at the time of the onset of the fever while he was still shivering.

No flagella were found in this case although several specimens of the blood were examined daily.

The weight in this case went down about 10 pounds, and in another Quartan case of the severe type the weight went down 12 pounds in a fortnight. In the group of what we have called the *clear* Quartans, that is those with regular paroxysms every third day and with no fever on the intervening days, it will be seen that the weight sometimes actually increases during the time that the paroxysms are occurring.

*Case II—Domia.* Had five turns of fever before he came to Hospital and he had 5 turns while in Hospital. The chart shows the high, lower, and low temperatures on the first three days. The fever stopped without quinine in this case, and this is unusual in Quartans.

The following is an extract from the daily notes:—

*16th.*—The two-day old parasites are seen filling two-thirds of corpuscle.

*17th.*—Fever is expected to-day: at 1 P. M. he feels cold: four very perfect rosettes seen, they are circular in form and the pigment is in the centre. One parasite has advanced to a further stage and has lost its circular form. The spores are lying irregularly around the pigment which is not quite central. Another parasite is not yet full grown and there is a little bit of the corpuscle which has not yet been consumed.

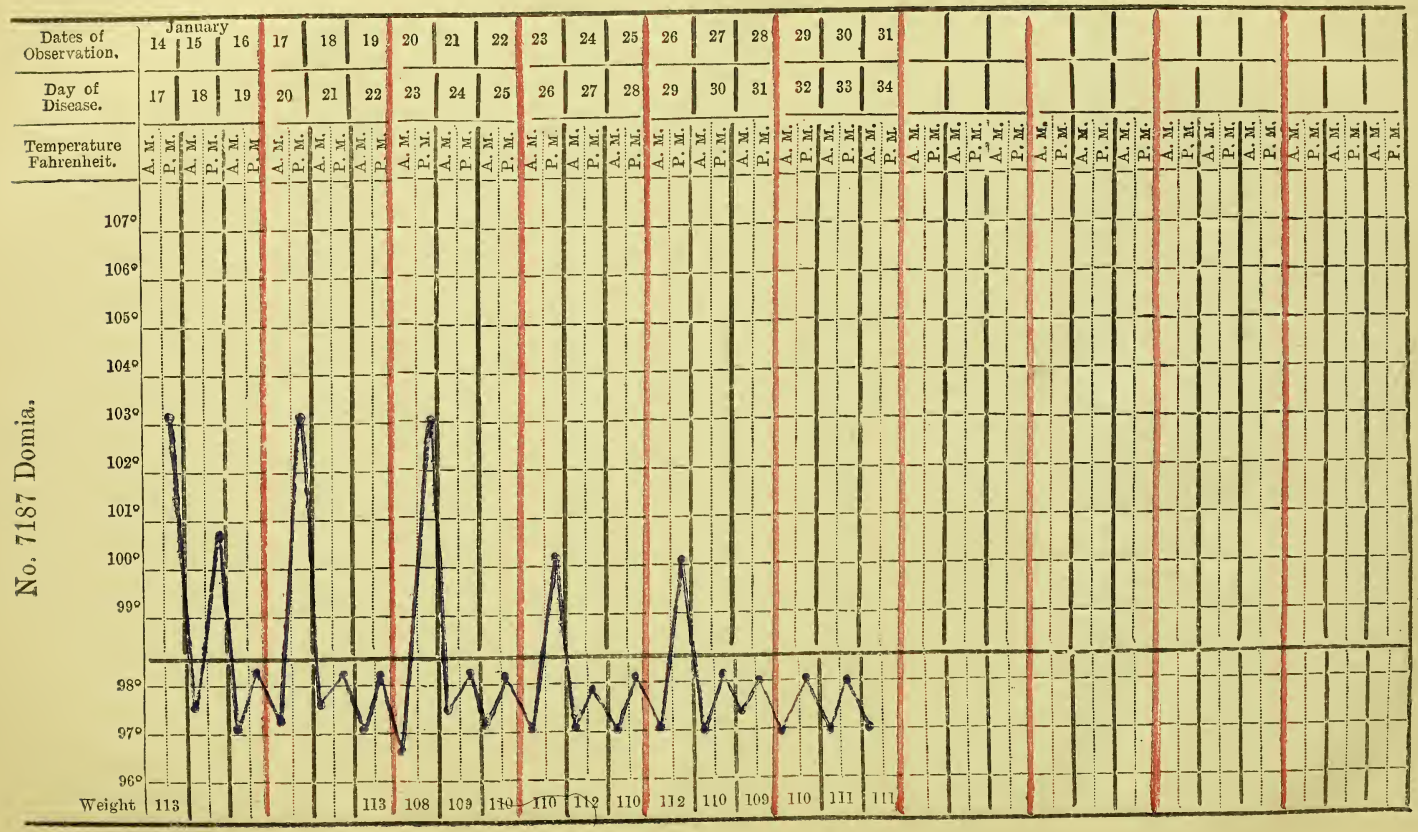
2 P. M.—Shivering severely: temperature 100·4, a good rosette seen, the nuclei of the spores clearly seen, but the spore circles not yet completed.

4 P. M.—Temperature 103: several broken rosettes seen: in one field as many as three seen.

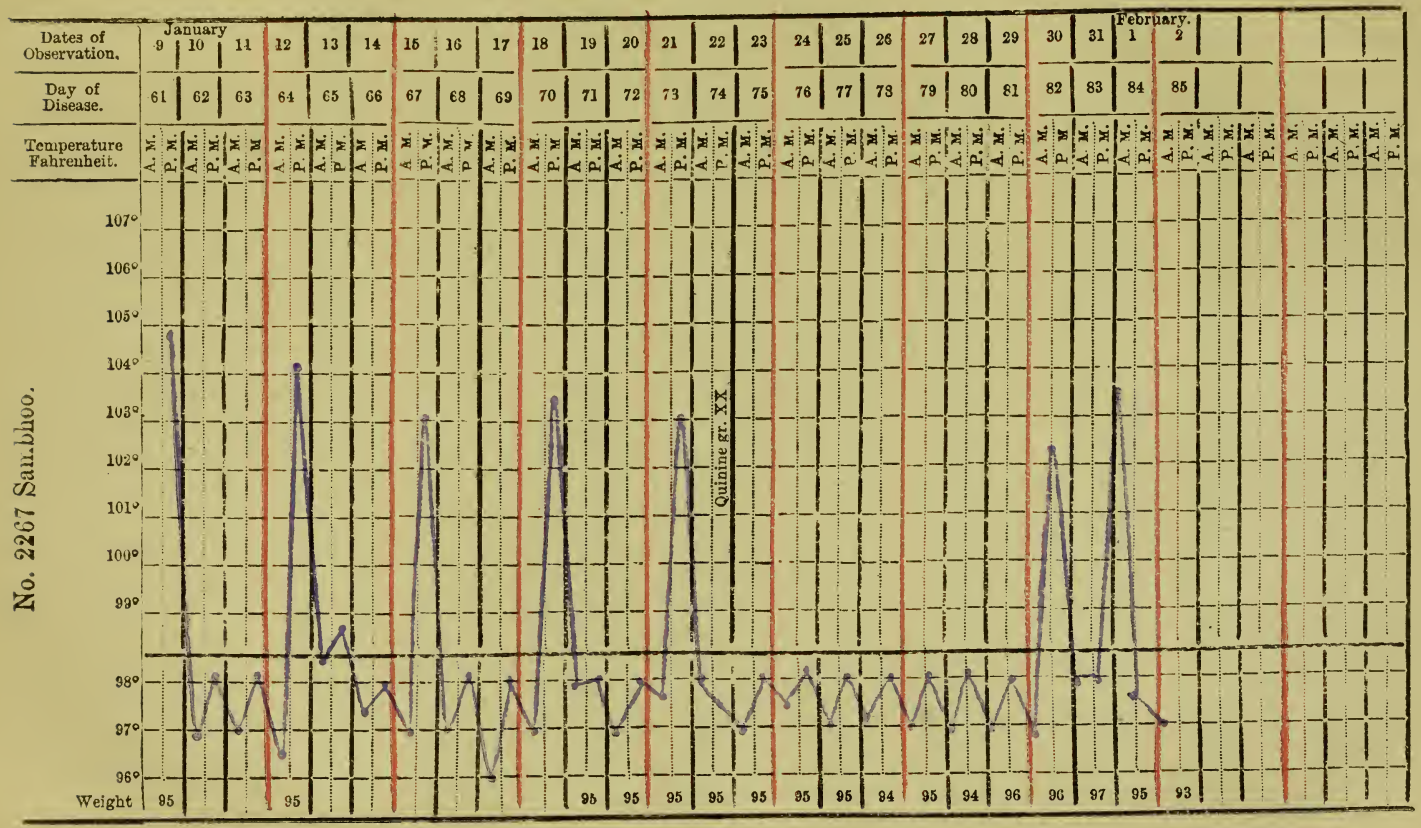
4-15 P. M.—A young form seen in a corpuscle and there is a minute speck of pigment in it, so it would seem that the young forms invade the corpuscles before the sweating stage has begun.

On the 23rd, one of the days for fever, a rosette was found in blood drawn before the shivering, but no rosettes were found in the blood drawn at the time of shivering. Some hundreds of specimens of blood from Quartan cases have been examined at the time when the shivering begins, and on only this one occasion did we fail to find rosettes.

# QUARTAN CHART



# QUARTAN CHART



*Case III.*—Three charts are given to show cases of "clear" Quartan. *1st—Sambho.* In this case after 5 paroxysms of fever there was no loss of weight. Quinine (grains xx) was given on the day after a paroxysm, that is when the young parasites were one day old. The parasites soon disappeared and the paroxysms stopped for a time but they began to come on regularly again a month later. Some one who was visiting the Laboratory said perhaps arsenic has a good effect in some cases and has not such a good effect in others and that quinine may have a better effect in some cases than in others. It was decided that the effects of arsenic should be tried in this case.

(As the number of charts already reproduced is rather large another method of illustrating the fever will be adopted. The degree of fever will be represented by figures showing the number of degrees above normal. Thus a temperature of 103·4 will be indicated by the figure 5, that is, 5 degrees above normal. Decimals will be omitted and the nearest whole numbers will be given. There was practically no rise of temperature on the intervening days so the temperatures on these days will not be put down. Further, only the highest daily temperatures will be entered.)

| Date. | Feby. 21 | 24 | 27 | Mar. 2 | 5 | 8 | 11 | 14 | 17 | 20 | 23 | 26 | 29 | April 1 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Degrees of fever. | 5 | 4 | 4 | 4 | 3 | 4 | 3 | 6 | 6 | 0 | 4 | 4 | 5 | 6 | Quinine. |
| | Liq. arsenicalis m. v, thrice daily. | | | | | | | | Liq. asenicalis ½ drachm daily. | | | | | | |

This case illustrates the remarkable persistence of Quartan. The paroxysms kept on steadily recurring for 40 days. Arsenic was given and the dose was increased until half a drachm was being taken daily. The temperatures were on the whole higher while the large doses of arsenic were being given, and the parasites were found regularly.

Quinine (grains xx) was given on the 2nd of April, and on the 4th April no parasites were found and the paroxysms stopped.

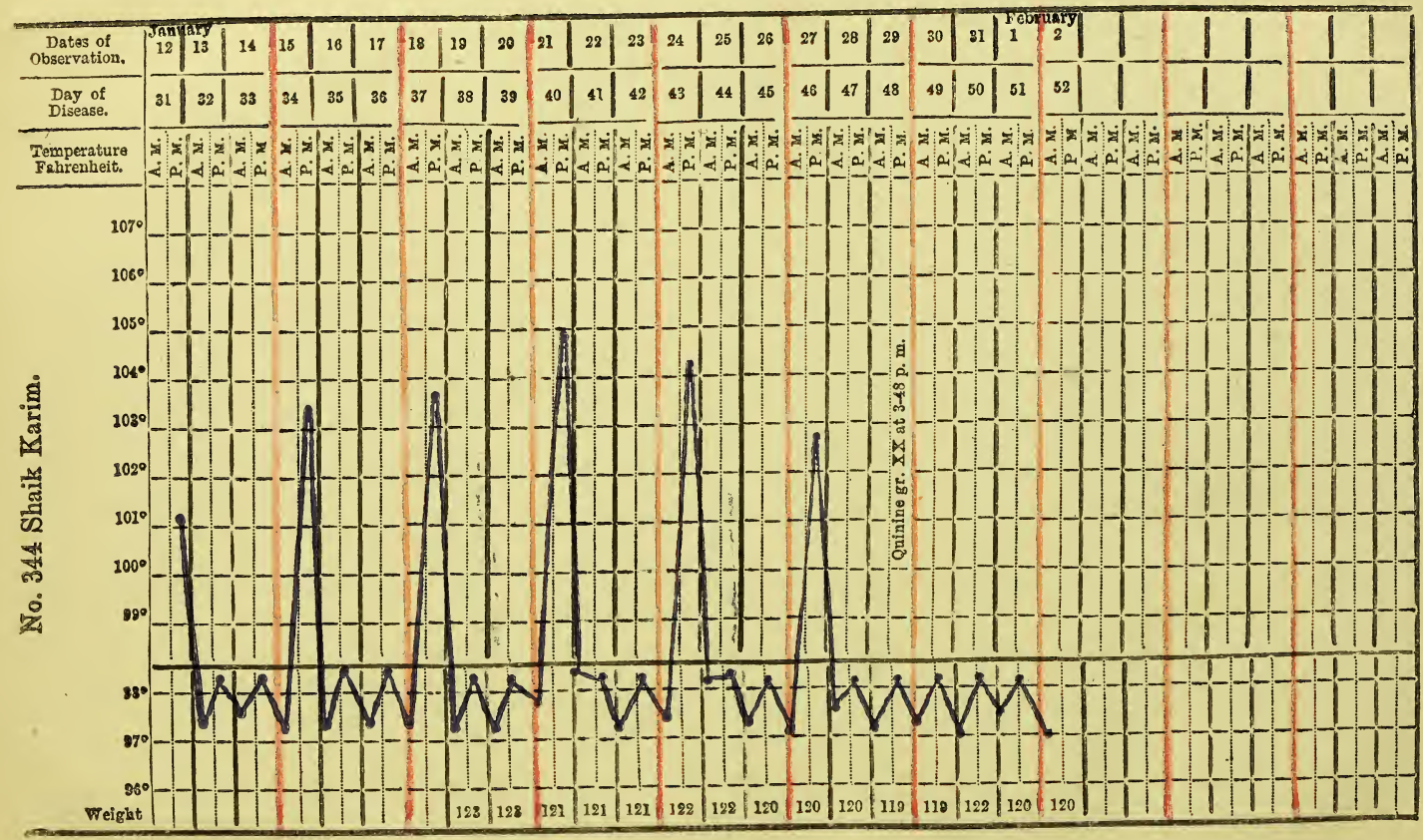
*Case IV.*—Shaik Karim's chart shows 6 turns of clear Quartan. Quinine (xx grains) was given when the parasites were two days old, and next day (30-1-01) the following note was made :—

> " The blood was examined this morning and Ko Tha Aung reported that one parasite was seen but the pigment was not moving. I saw one parasite in this specimen and confirmed the observation. At 2 P. M. the blood was examined again. After a long search I found only one parasite : it did not fill the corpuscle and the pigment was not moving. Now at 2 P. M. we can confidently say that his fever will not come to-day.
>
> 31-1-01.—No fever came last night, and after a prolonged search no parasites could be found."

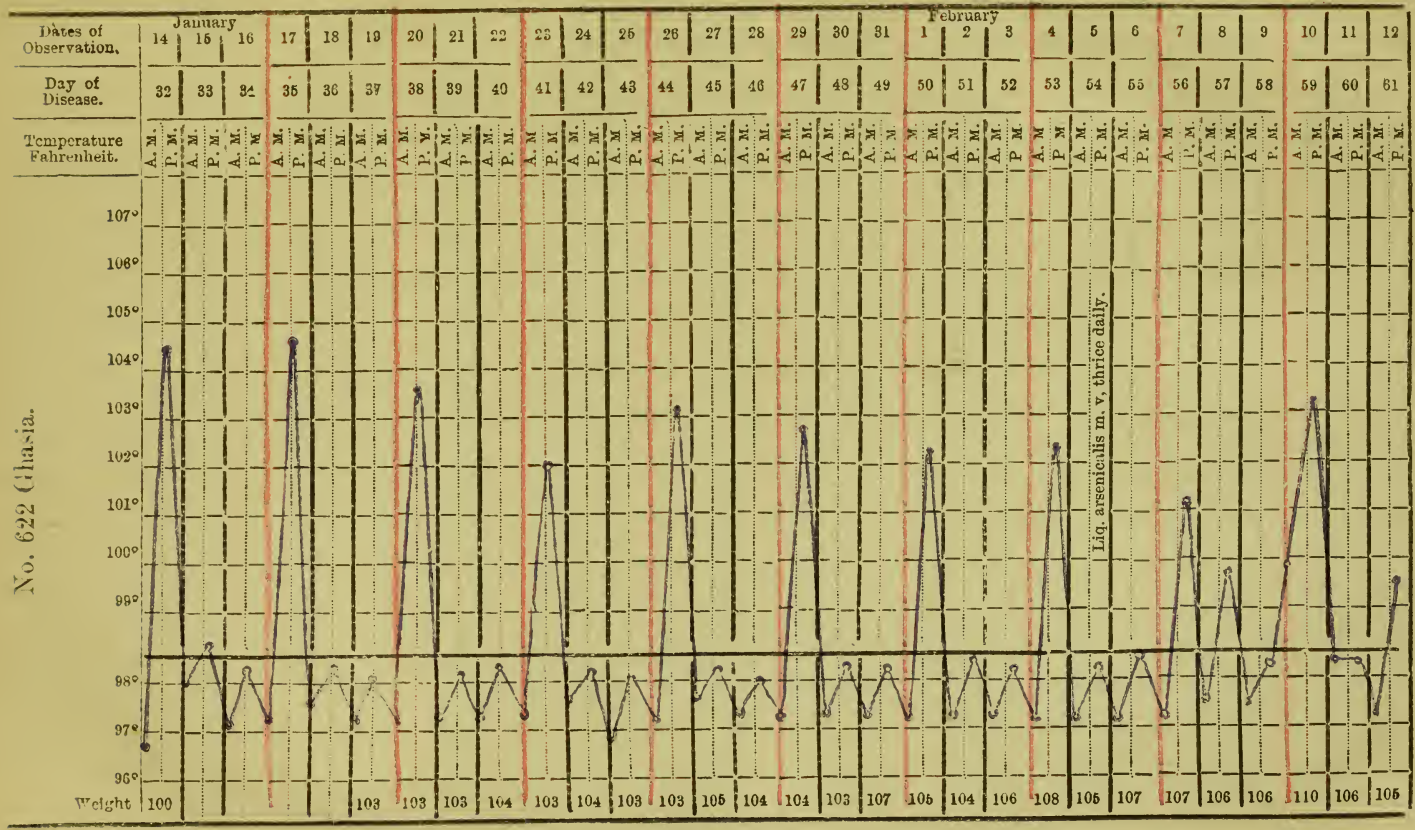
*Subsequent note.*—From the 27th January till the 4th March no fever came. Then paroxysms began to come regularly. After 6 paroxysms in which the temperature went up to 103° or 104° twenty grains of quinine was given. Two Native gentlemen happened to visit the Laboratory on 20th of March and in the course of conversation they said that Quartan fever is very persistent and that it does not yield to quinine. We offered to give them a hundred rupees if the paroxysms were not stopped by the one dose of quinine in this case. The quinine was given on the 20th : on the 21st, 2 parasites were found, but the pigment was not moving : on the 22nd, which in the ordinary course would have been the day of fever, no parasites were found, and we were able to say with certainty that the fever would not come on that evening. Twenty days have elapsed and the fever has not returned. Probably a small dose of quinine would not have had the same effect in stopping the fever, and this may explain why the Native gentlemen were of opinion that Quartan fever is not stopped by quinine.

It may be noted that in this case and in the preceding case the fever returned about a month after one dose of quinine was given.

# QUARTAN CHART



# QUARTAN CHART.



*Case V.*—Ghasia had been getting Quartan fever for nearly a month before he reported sick. On the morning of the 14th, the day after he came to Hospital, the following note was made :—

> " I see nearly full grown parasites. Why should we find full grown parasites now ? Yesterday he says was his day for fever. Stained specimen very good—full of parasites, nearly all full grown."

His fever came on that same evening at 8 o'clock so that his statement that the 13th was his day for fever was wrong. True, he had had some fever, but it was slight as compared with the high fever on the regular day. This illustrates how the size of the parasite indicates its age.

In this case the effect of arsenic was tried. Liquor arsenicalis in 5 minim doses was given thrice daily, beginning on the 6th February. On the 10th the temperature was higher than it had been for a fortnight. The remainder of the chart has not been printed, but it shows slight fever on the 13th, and no fever on the 16th. On the 14th the dose of Liquor arsenicalis was doubled, and it might seem that the absence of fever on the 16th was due to the arsenic ; but on the 19th, 22nd and 25th we find the fever going higher and higher on each successive turn so it may fairly be inferred that the arsenic has not the slightest influence on the Quartan parasite.

The weight of the patient increased by about 7 pounds while the fever was going on.

*Quartans combined with other parasites.*—We now come to the group in which Quartan parasites are found together with other Malarial parasites. To illustrate this group two charts will be given. In both of these Quartan parasites, as well as the parasites of Malignant Tertian were found. In both of these the temperature was irregular at first and in both the parasites of the two kinds of fever were found a day or two after admission to Hospital. In both the Malignant Tertian disappeared early, and as the Malignant Tertian parasites disappeared the Quartan nature of the fever became more distinct. The paroxysms in the early time in both were mild and later they became more severe.

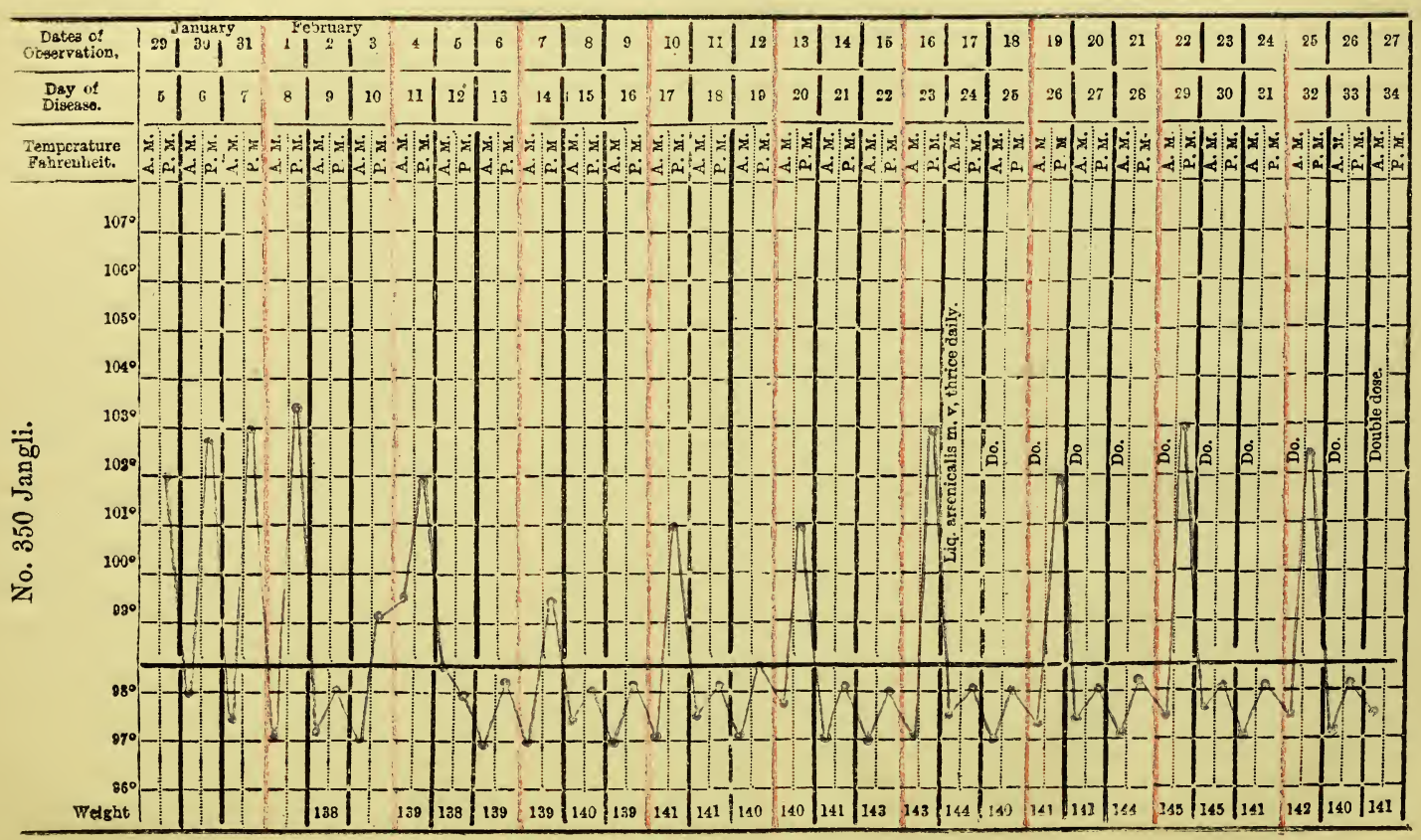
*Case VI—Jangli.* In this case Quartan and Malignant Tertian parasites were found. The temperature at first had a Quotidian appearance—another proof that the chart for purposes of diagnosis is not reliable.

This case also illustrates the persistence of Quartan fever.

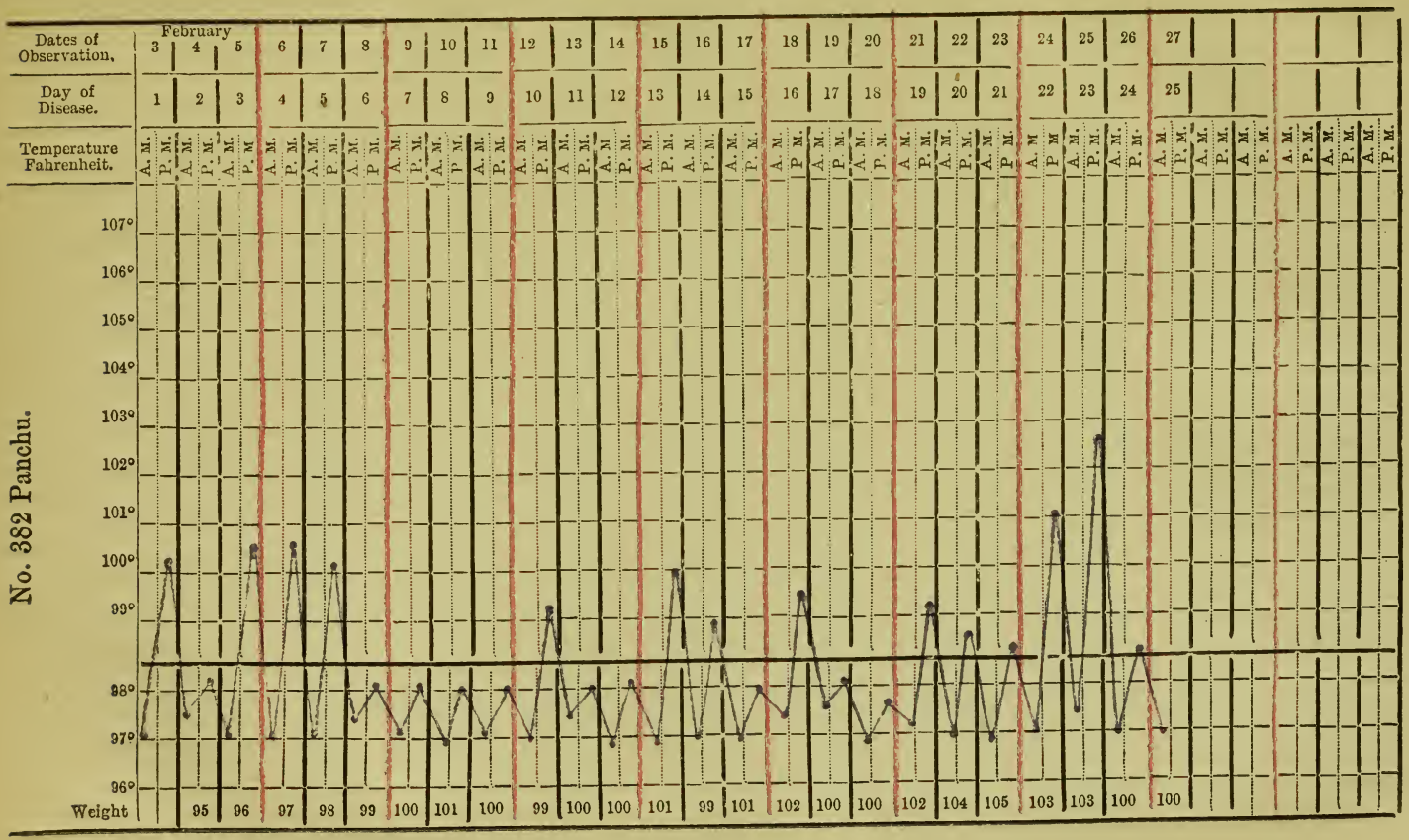
It also illustrates what has been already said about arsenic. Five minims of the liquor arsenicalis were given from the 17th till the 27th. The dose was doubled on and after the 27th. 5 paroxysms came after the arsenic was begun, and the temperature in the last but one paroxysm was higher than it had been for a month before.

The weight increased a few pounds while the Quartan fever was going on.

# QUARTAN CHART. + MALIGNANT TERTIAN.



# QUARTAN CHART. + MALIGNANT TERTIAN.



*Case VII, Panchu.*—Quartan and Malignant Tertian parasites were found in this case. Only a few of the Tertian parasites were present. After seven Quartan paroxysms a Native medicine called "*atthis*" was tried, and experiments with it are being made at present.

In this case the weight went up over 5 pounds.

*Subsequent note.*—Five paroxysms occurred after the *atthis* was begun. The amount of *atthis* given was 20 grains three times daily and this dose was continued for about three weeks.

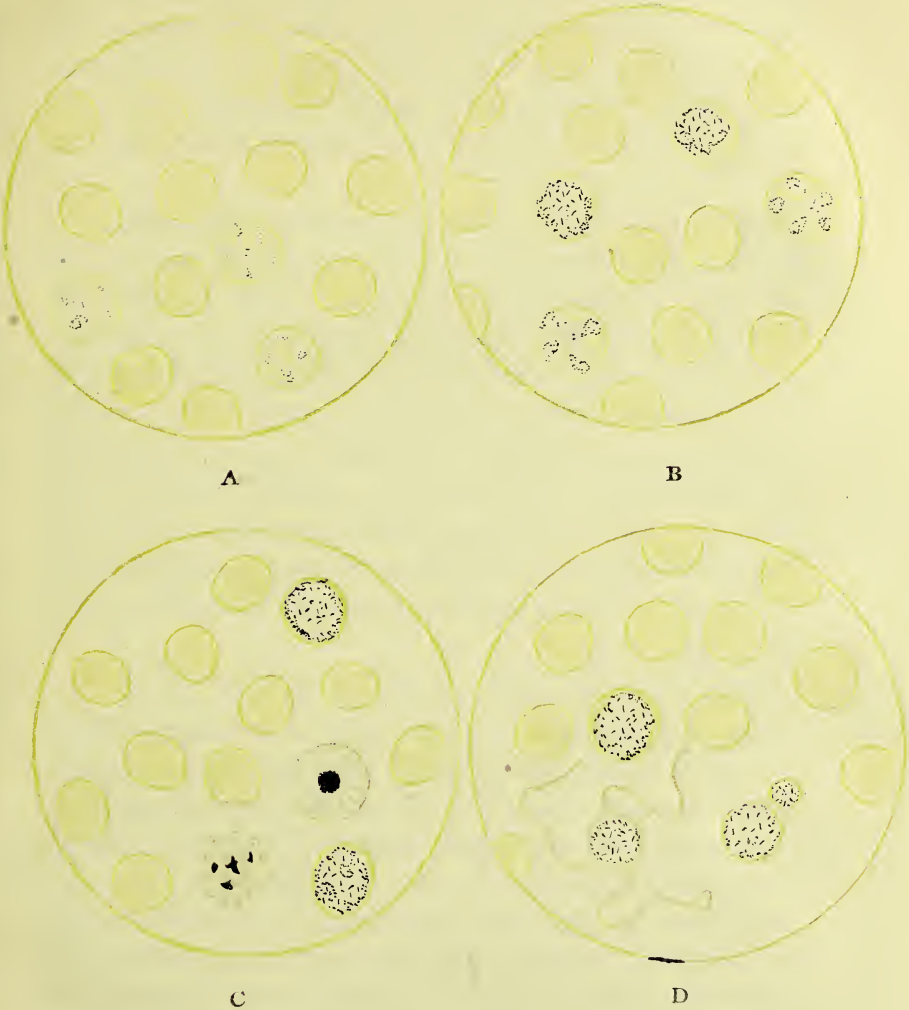
# CHAPTER V.

## BENIGN TERTIAN PARASITES.

In the tabular statement which is given at page 9 the differences between the Quartan and Benign Tertian parasites have been briefly explained. The young forms of the Benign Tertian are very characteristic. Before they are pigmented they move more actively than the Quartans, but this difference in movement would not enable us to make a differential diagnosis between these two kinds of parasites. After the pigment has begun to form, the Quartan settles down and there is not much activity in the movement of the pigment. The Benign Tertian however still continues its amœboid movements. It is, if the expression may be used "all arms," and the ends of these arms are often slightly enlarged. The pigment is collected in these terminal enlargements and it would appear sometimes, at first sight, as if there were 3 or 4 small parasites at work in different parts of the red blood corpuscle (A).

If we watch them however for a few minutes it will be seen that they are connected together and these arms will be drawn in towards the main body if such can be said to exist (B). This appearance is very characteristic, and it is quite enough to justify a diagnosis of Benign Tertian. The red blood corpuscle soon after it has been invaded becomes enlarged and clear in colour. At this early stage the pigment in the Benign Tertian is not in rods, or at least rods cannot be as distinctly seen as they can be when the parasite is full grown.

## BENIGN TERTIAN PARASITES.




A. Young forms.
B. Half grown.
C. Full grown : forming Rosettes.
D. One full grown : one throwing out flagella and one divided into two spheres, prior to exflagellation.

Opposite page 26.

When we watch one of these young forms free in the plasma two parts can be seen especially if the specimen is stained. One part takes a blue stain, the other part which looks like an empty sac does not take the stain except at the circumference.

Rosettes are seen frequently but not as frequently as in the Quartans. There are about 20 parts in the rosette, but it should be remembered that it is only after a rosette has become a little broken up that it is possible to count the number of parts, and if we should see a young rosette it would frequently be impossible to say definitely whether it is a Quartan or a Benign Tertian. If it is a little broken up and the spores are not held together inside a circular capsule then it may be possible to say definitely which form of fever the parasite belongs to (c).

In an Article by Major Melville, R. A. M. C., which appeared in the *Indian Medical Gazette* in March 1899, he says "There was an attempt to distinguish between the Tertian and Quartan forms, which in ordinary clinical work must, it appears to me, be impossible in the absence of 'rosettes.'" Major Melville does not say what kind of tertian he is speaking of, but if it is the Benign Tertian, it is curious that one of the first things we show new men here is a Benign Tertian and a Quartan and we find that they can learn to distinguish between these two in a few minutes *provided the parasites are not in the rosette stage.*

The Rosette generally forms after the whole of the invaded corpuscle has been eaten up by the parasite,

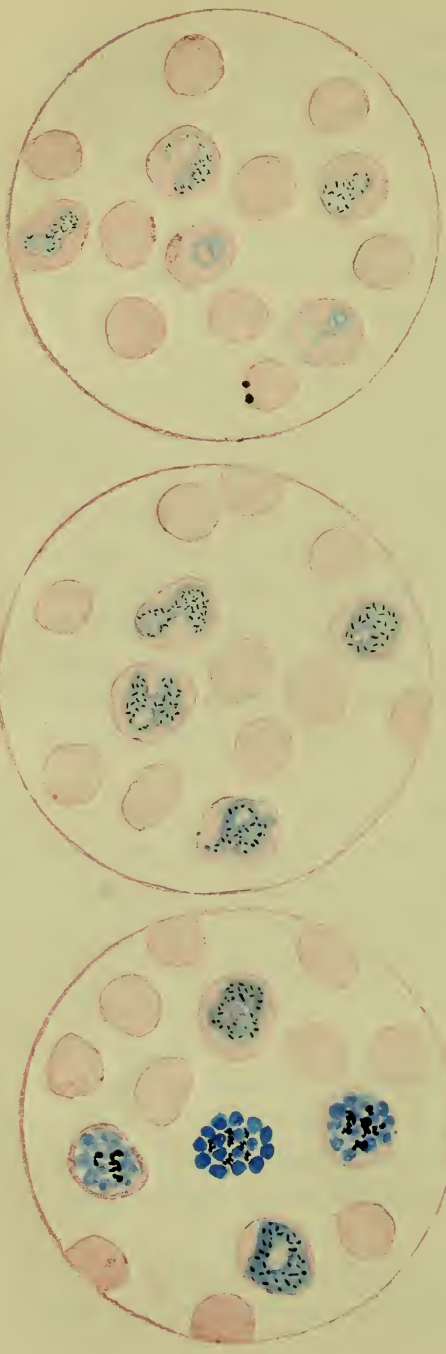
but this is not always the case, and we frequently see, especially in stained specimens, a Rosette with a part of the original corpuscle still beside it. This is very uncommon in Quartans.

Flagella are not often seen in Benign Tertian cases. When we are describing the Malignant Tertian fever we shall explain how the flagella appear at a certain period—during what we have called the "flagellar fever." We are not certain if the flagella appear at a more or less definite time in the Benign Tertian, but although we looked in all the cases of what appeared to be first infections flagella were not found while the paroxysms continued. In two cases in which flagella were found the primary paroxysms had stopped for some time. The men again came to Hospital and flagella were then found. It would seem that there is a Secondary fever in which the flagella are found (D).

There is a curious contrast between the two Tertians as regards their influence on the invaded corpuscle. The Benign parasite causes the invaded corpuscle to swell whereas the Malignant Tertian parasite often causes the invaded corpuscle to undergo a kind of crenation. We often see a field in which all corpuscles but one are crenated and that one has a Benign Tertian parasite inside; and we often see a field in which only one corpuscle is crenated and that one holds a Malignant Tertian parasite—it is the Brassy body of the Italians.

The pigment is in rods, but it is difficult to see the rods of pigment in young forms, and even in full grown

BENIGN TERTIAN PARASITES STAINED.



A. 1st day: young parasites, some with pigment and some without pigment

B. 2nd day: pigmented parasites

C. 3rd day: full grown parasites and rosettes forming when fever is coming on.

forms sometimes, owing to the rapidity of their motion. The rods are best seen in stained specimens. In some stained specimens we see the rods of pigment on the slide, but the body of the parasite has apparently disappeared.

# CHAPTER VI.

## BENIGN TERTIAN FEVER.

THERE are two malarial parasites which take 48 hours to complete their asexual cycle of development. One is called the Benign Tertian and the other the Malignant Tertian. The latter is called Malignant because the paroxysms of fever may be "prolonged and approach each other so as to simulate a continued fever" (Celli, page 46). Some charts of both these kinds of fever will be given and it will be seen that although these two kinds of fever resemble each other in as a rule giving a higher temperature on alternate days, the charts otherwise show very marked differences. The two most curious points about the Benign Tertian fever are :—

(1) the tendency for the paroxysms to recur, and

(2) the tendency for the temperature to run up high.

The first chart shows about 10 paroxysms and the fever was then stopped by quinine. The second shows about 13 paroxysms and the fever was then stopped by quinine, as the patient got a Malignant Tertian infection in addition to the Benign. The third shows 6 paroxysms and then it presents some irregularity. The fourth case shows only 4 paroxysms. Now when we compare these with the Malignant Tertian charts it will be seen that the Malignant chart nearly always shows a downward tendency a "slope downwards."

The other point is that the fever frequently runs up very high in the Benign Tertians: temperatures of 105 or 106 are not uncommon. (See the charts of Thibroo, Narayan, and Sheik Gulab.)

We have said that these are the two most curious points about the Benign Tertian fever, because it may seem extraordinary that the Tertian which has the higher temperatures and in which the paroxysms are most likely to be repeated should be called "Benign." But there are other points that have to be considered. The duration of a paroxysm is much shorter in the Benign Tertian: there is a severe shivering fit, a rapid rise of temperature, and this is soon followed by free perspiration. On the intervening days it is rare except in the first few days of the fever to get a rise of temperature, whereas in the Malignant Tertian the temperature is often high on successive days. Then if we look at the weights we find that the weight rarely falls more than a pound or two in Benign cases and in some the weight has actually increased.

In Quartan fever it is very rare to find the day of fever changing, that is, if it comes on the 6th, it will come on the 9th, 12th, &c., but in the Tertians we sometimes find a change of day. If the fever has been coming on the 3rd, 5th, 7th, it may then come on the even days—the 8th, 10th, &c. This change is seen in both the Tertians. It is interesting to note that in the Tertian fever of sparrows there is often a change of day.

The charts of 4 cases will be given—one chart each for the first three. The fourth case was a very long one, and as there were altogether four admissions to Hospital—apparently as a result of one infection—two charts are given to illustrate this case.

*Case I, Sheik Gulab.*—This chart shows a fairly regular rise of temperature on alternate days. Note that the temperature was 105·6 on the day of admission. The day of fever did not change. After the 10th paroxysm quinine was given and the fever stopped. The loss of weight was 3 lbs.

*Case II, Thibroo.*—Note that the temperature on two successive days was over 106. Then for two days there was no fever and the chart after this shows a regular Tertian appearance. On both days, when the temperature was high, many "boilers," that is, parasites with the pigment moving rapidly were seen. There appears to be some irregularity in the fever on the first few days of Benign Tertians. The chart may show a Quotidian appearance even though there is not a double infection.

*16th December.*—Many phagocytes seen: they seem rather dark in colour: 3 seen in one field.

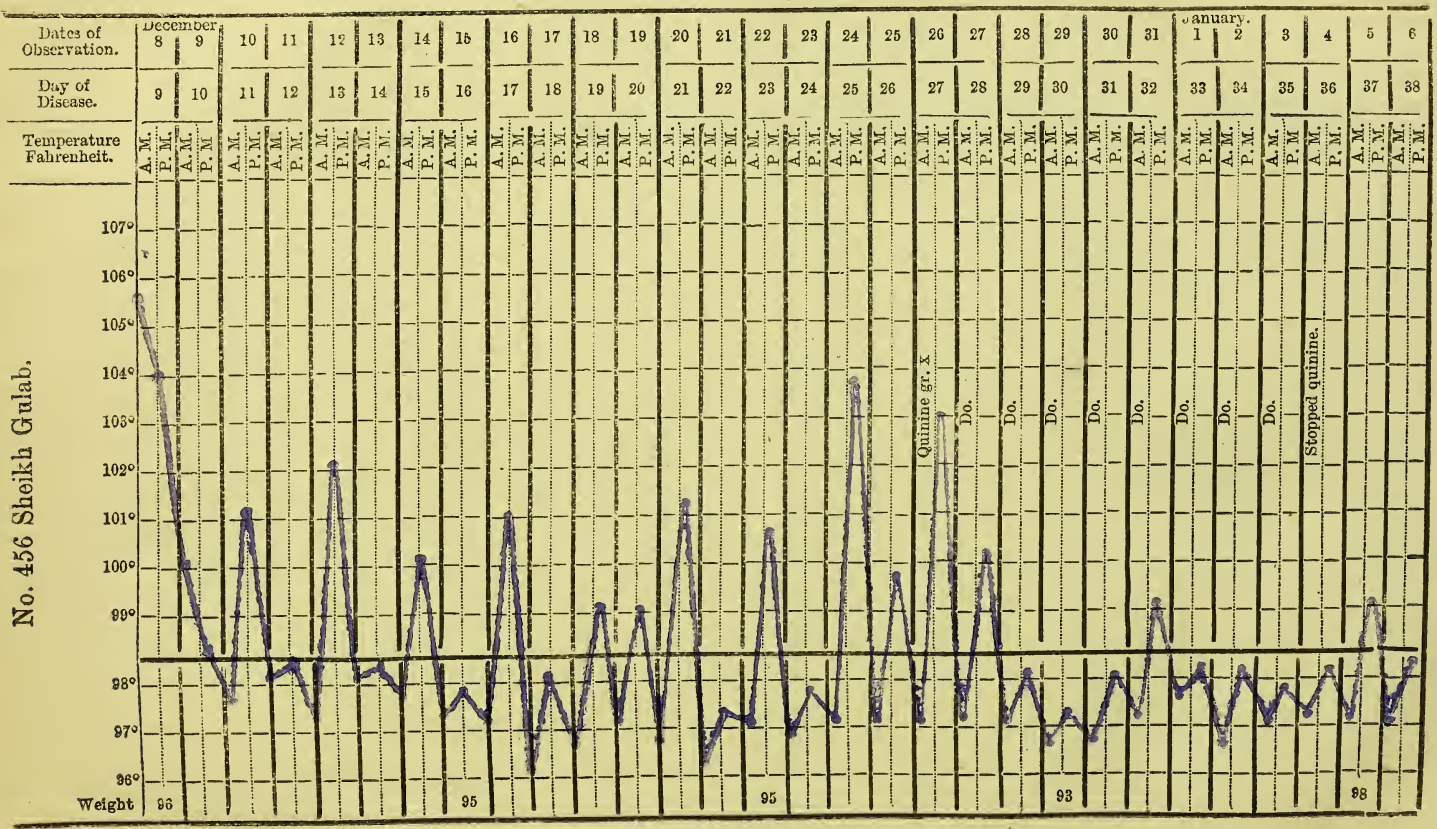
*27th December*—The large clear cell which the parasite has invaded is not crenated although all the other red blood corpuscles in the same field are crenated. His fever stopped without quinine.

Towards the end there is an attempt at a change of day.

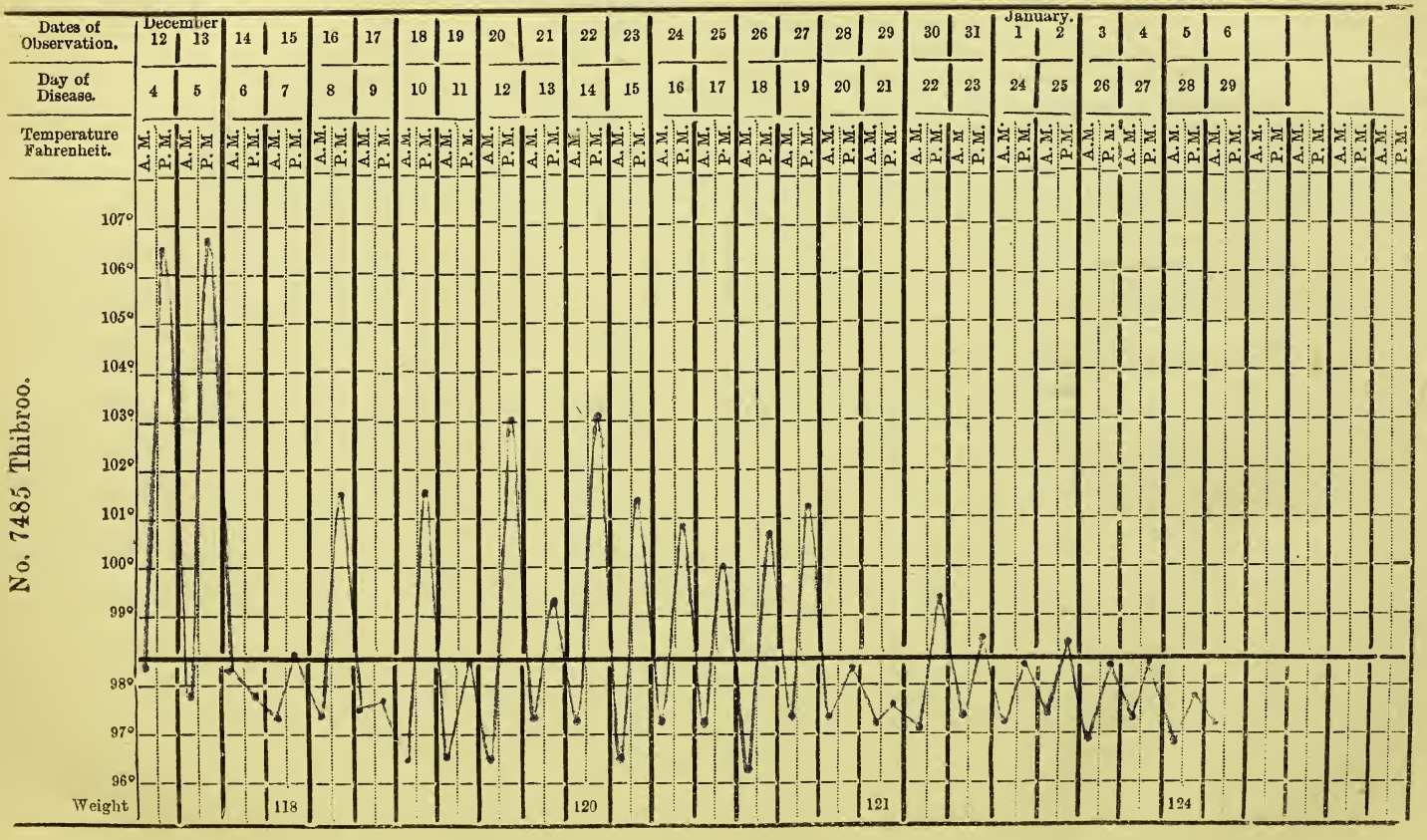
*Case III, Yeshwanta.*—He had 4 paroxysms of regular Tertian, an interval of 11 days without fever and was discharged on the 15th February. He was again admitted on the 27th February with slight fever and several flagella were seen. He had also crescents as well as Benign Tertian parasites and both kinds of flagella were seen.

*3rd March 1901.*—Although many Benign Tertian parasites are found in the blood and also crescents he has not had fever for a few days.

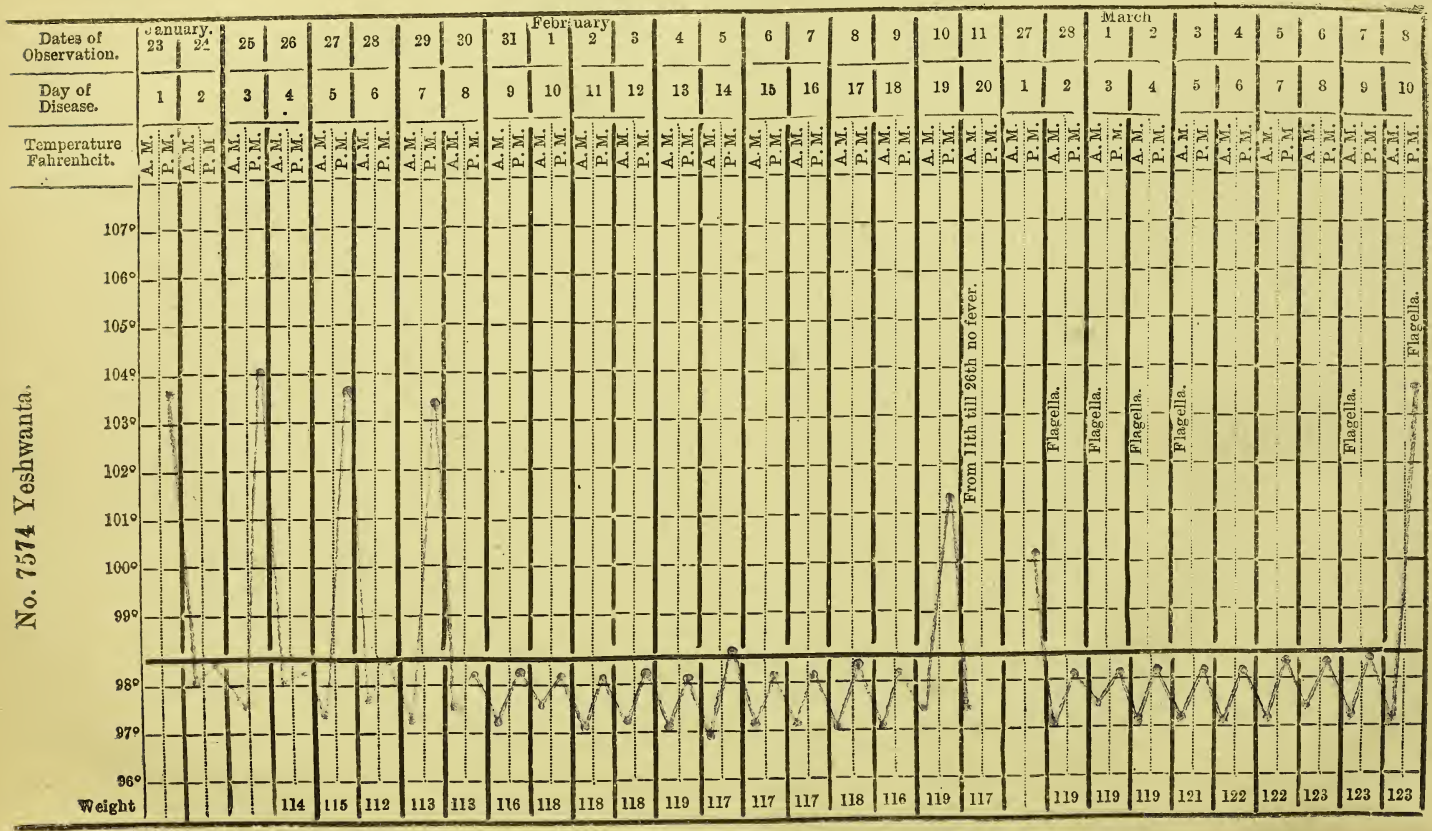
# BENIGN TERTIAN CHART.



# BENIGN TERTIAN CHART.

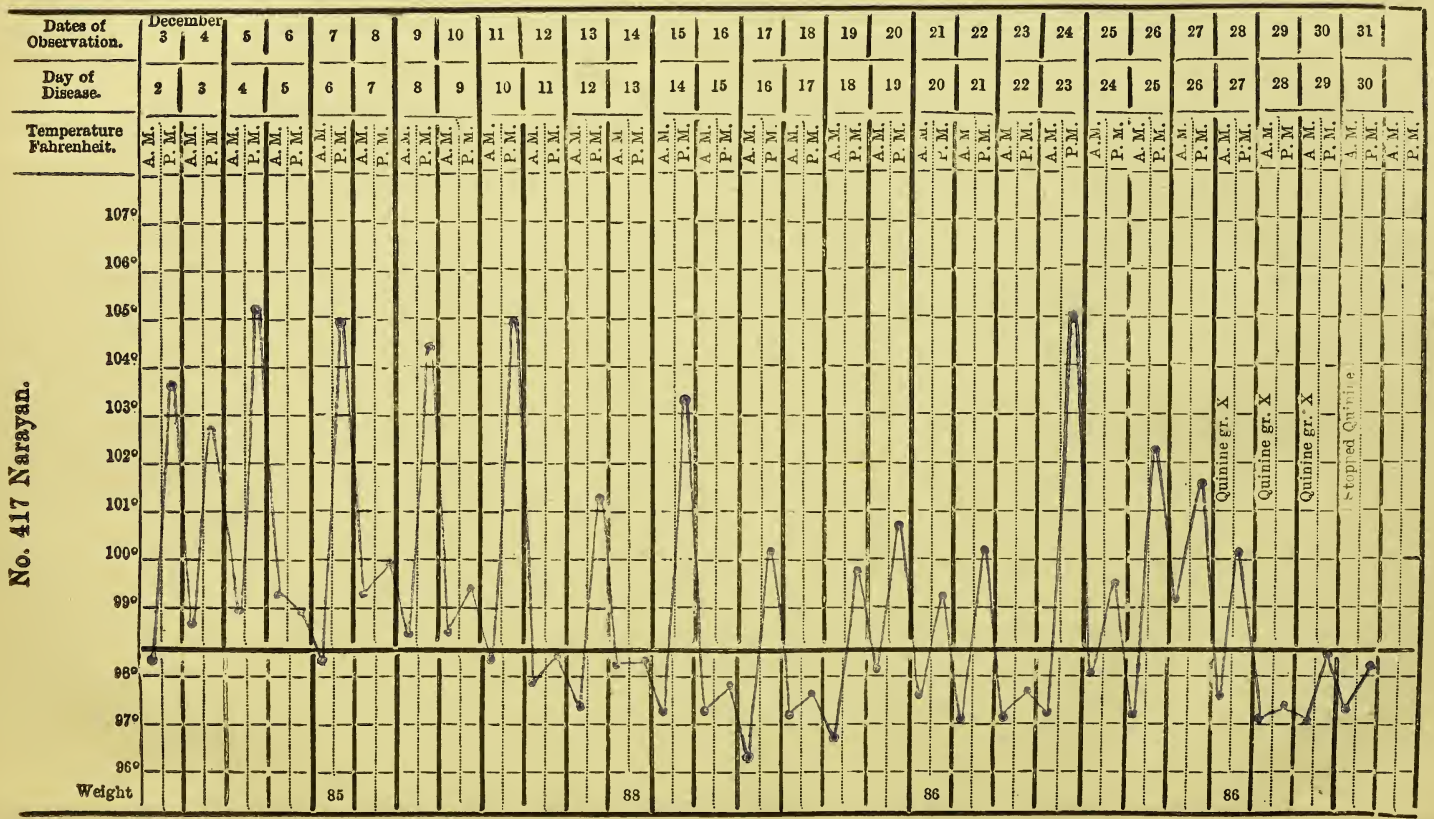


# BENIGN TERTIAN CHART.



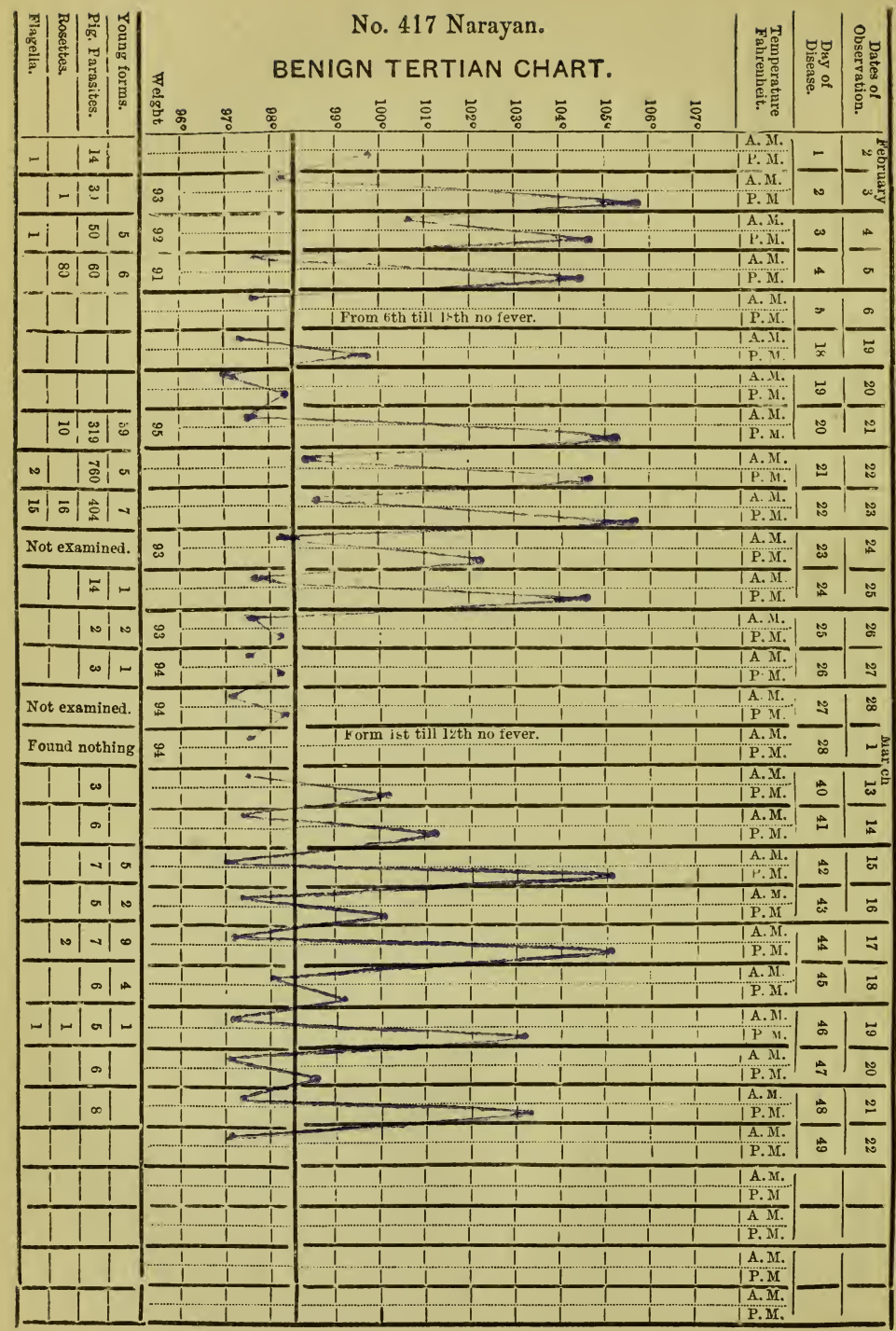

No. 7574 Yeshwanta.

# BENIGN TERTIAN CHART.



# No. 417 Narayan.

## BENIGN TERTIAN CHART.



*Case IV, Narayan.*—Two charts are given to illustrate the temperature in this case and the second chart represents three separate admissions to Hospital.

*1st admission.*—After 9 turns of fever the day changed and the fever which was coming on the odd days of the month began to come on the even days. He then got a Malignant infection and crescents were found. Quinine was given. He was discharged from Hospital on the 24th January and was again admitted on 2nd February.

*2nd admission.*—There was fever daily for four days but the chart shows no appearance of Tertian although many Benign Tertian parasites were found.

*3rd February 1901.*—In blood drawn to-day (temp. 105·6) we see an enormous number of young parasites. In one field I counted one young ring form, eleven pigmented parasites, and one very nice rosette in which the pigment is central and the nucleoli are seen distinctly. Outside there is a small rim of ground substance.

*4th February 1901.*—This morning a parasite was seen giving out flagella and we watched it for half an hour. This is an unusually long time for flagella to continue moving. A phagocyte then came. The temperature was 102·6 when the blood was drawn.

From the 6th to the 18th there was no fever. On the 5th a large number of parasites were counted. In one slide which had been kept for a few hours 40 rosettes were seen. It seems curious that no fever should have followed although so many rosettes were found.

*3rd admission*— Here the chart shows a Tertian appearance though not a clear Tertian. The number of parasites seen was very remarkable : on the 22nd as many as 767 were counted in ten slides—twenty minutes being devoted to the examination of each slide. Fifteen flagella bodies were seen on the 23rd and the question arises whether there is a Flagellar period in Benign Tertian as there is in Malignant Tertian cases. From the 26th February to the 12th March—an interval of 15 days—there was no fever excepting on one day and then fairly regular Tertian came on.

*4th admission.*—Here one flagella body was found and the majority of parasites seen were of the ordinary kind.

# CHAPTER VII.

## MALIGNANT TERTIAN PARASITES.

This is also called the Aestivo-autumnal fever or Summer-autumn fever. Before describing the nature of the fever as illustrated by the charts, a short account of the appearance of the parasites will be given In this fever we see the parasites in four very distinct stages or conditions, *viz.* the young forms (unpigmented and pigmented,) the crescent bodies, the flagella bodies, and the rosettes. These will be dealt with in succession.

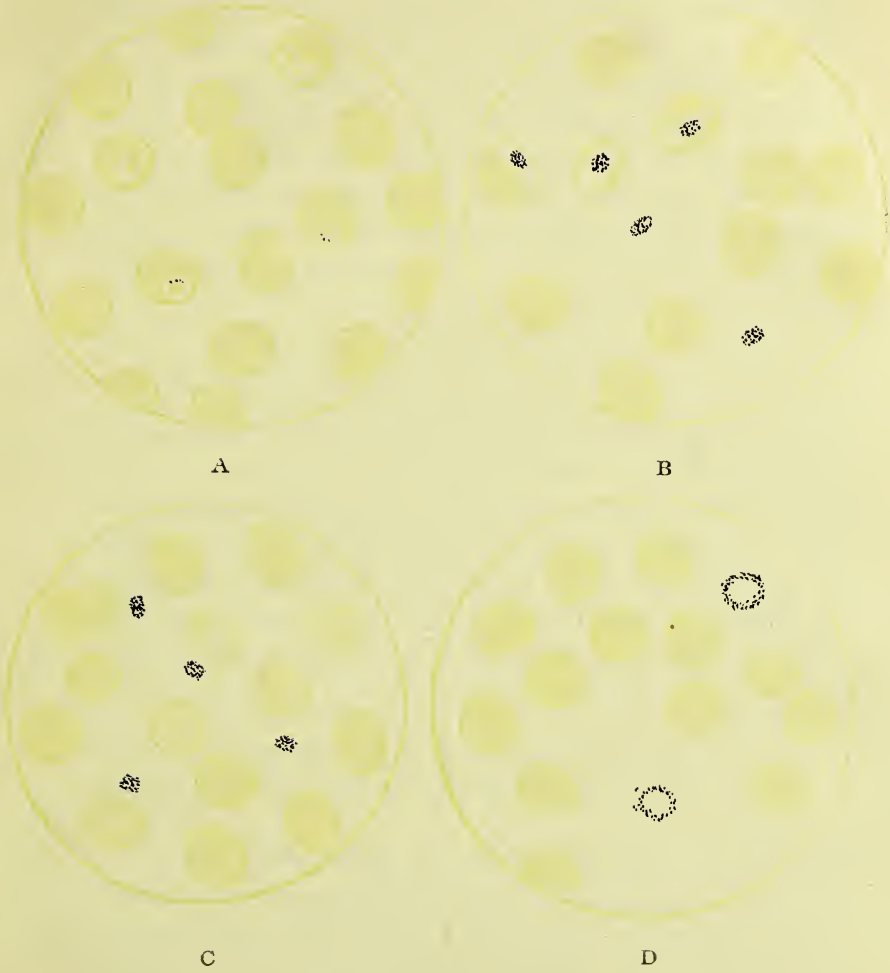
### Young Forms.

When unpigmented the young forms move inside the red blood corpuscles very much in the same way as the young forms of the other parasites, but this motion soon ceases and they are seen in their very characteristic shape as "Ring forms." The ring is colourless, and inside the ring is a disc which has the same colour as the red blood corpuscle. (A)

Pigment forms early and it will be seen in the ring part, but note that it is always small in amount, and usually there are not more than two or three granules of pigment. (A)

The invaded blood corpuscles sometimes lose their shape and undergo a sort of crenation, forming what have been called by the Italians "Ottonati" Brassy bodies. One often sees only one crenated corpuscle in a field under the microscope and that one

# MALIGNANT TERTIAN PARASITES.




A. Young parasites: 2 Ring forms.
B. Crescents forming: in the very early stage the corpuscle has not lost its colour: in the later stage all colour has gone from the belly part and only the boundary line can be seen.
C. Crescents fully formed. Note how they often lie close to a corpuscle.
D. Flagella body or gamete throwing out flagella and one ? female.

corpuscle will have a Ring form inside of it. These Brassy bodies soon disappear from the peripheral blood and remain in some internal organ for some days. It is said that they go to the spleen and to the bone marrow but this point has not been investigated here. When they next make their appearance in the blood they are in the form to which the name Crescent has been given. It should be explained that the Brassy body stage is not often seen.

### Crescents.

Owing to the fact that the Ring forms disappear from the peripheral blood when the crescents are about to be formed it is very seldom that we see the parasites in the transition stage. We have watched for it carefully but have only seen it on a few occasions. The Ring form lies at the side of the corpuscle; it becomes elongated, and one side of it lies in close contact with part of the circumference of the corpuscle.

For some days it apparently remains in the internal organs and when next seen it may be a crescent with a "belly" (B) or a fully formed crescent, (C)

The belly part is colourless and in unstained specimens we see only a very faint boundary line. It is sometimes difficult to see this belly part, but in stained specimens it can be readily seen, for it stains well with eosine, showing that it is the remnant of the blood corpuscle. We have particularly noted that this belly part is, in the unstained specimen, always absolutely colourless, except in the very early stage of crescent formation because in the first plate in Manson's

book this part is shown of the same colour as the red blood corpuscle but this is clearly not correct. The Malignant Tertian parasite destroys the colouring matter of the corpuscle while the crescent is forming. Now the Benign Tertian parasites early destroy the colouring matter of the red blood corpuscle, and we can easily understand how they may pick up this colouring matter as they are constantly sending out arms and retracting them ; but the crescent seems to fix itself to one side of the corpuscle, and without exerting itself much, it seems to draw the colouring matter from the corpuscle. The protoplasm of the corpuscle is afterwards gradually absorbed and then we get the typical crescent body. (C)

The pigment is usually collected in the middle of the crescent, and this pigment is in short rods. The pigment rods may be quiescent or they may be moving slightly. When blood containing crescents is drawn, we see at certain stages of the fever what are called

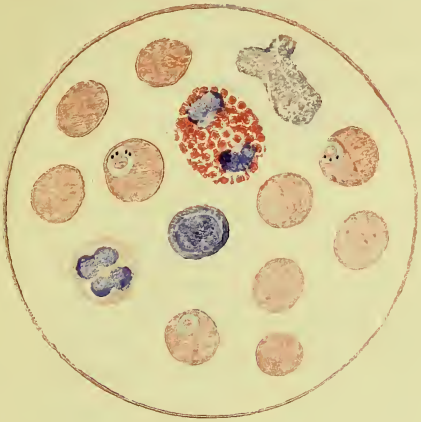
### Flagella Bodies.

The term "flagella" is applied to what appear to be the organs of locomotion of some microbes as the bacillus of Enteric fever or the bacillus coli.

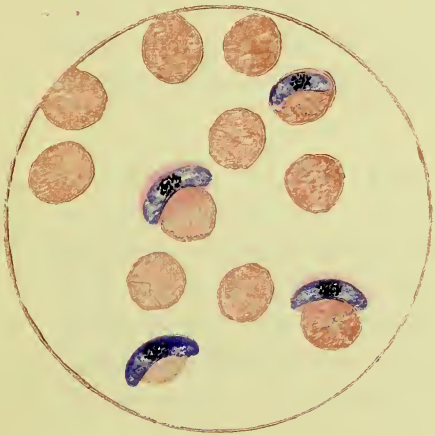
Enteric bacillus (diagrammatic)

and by a special method of staining the flagella of Enteric bacilli can be demonstrated. The flagella of

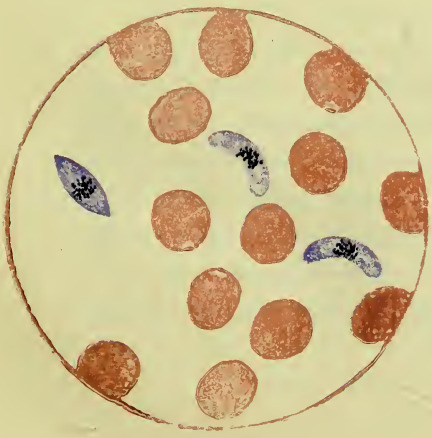
# MALIGNANT TERTIAN PARASITES STAINED.



A. Ring form: also from right to left a polynuclear cell: a leucocyte, an eosinophile cell: and a phagocyte



B. Crescents forming.



C. Crescents fully formed.

the malarial parasites are of quite another nature; they more resemble spermatozoa and it is well to bear this in mind as otherwise some confusion might arise from the application of the term flagella to organisms which are so totally different in their functions.

In stained specimens we see that some crescents take more of the blue stain than others. Manson quoting Bastianelli says the "male crescent stains more deeply" whereas Celli in his description of the female crescent says "the protoplasm is stained a darker blue." That some stain darker than others there is no doubt, but whether the darker stained ones are the males or the females, we have not yet been able to definitely prove.

If at a certain stage of the fever we watch crescents under the microscope we find some of them altering in shape and becoming round. This is the flagella body and in it we see an inner circle and an outer circle. The pigment is usually collected at the circumference of the inner circle and between the inner and the outer circle there is a clear space.

After a few minutes the pigment granules are seen moving——at first slowly, then rapidly. A few minutes later, if there are any blood corpuscles in the neighbourhood, they will appear to be very much disturbed, their edges will be turned up again and again, or a sort of shadow may appear to pass over some of them. What has happened or what has caused the disturbance? It is the flagella which have suddenly forced their way from the round flagellate body. (D)

No illustration can possibly give any idea of this very wonderful performance, for in the first place the flagella are as nearly as possible transparent, and in the second they are moving so rapidly that it is difficult and often impossible, to see them until their movement begins to slow down. If you could imagine half a dozen snakes tied together by the tails and all struggling vigorously to get free it would give some idea of the movement of the flagella. In the blood of the sparrow the flagella can be seen more readily and after breaking away from the flagellate body they can be seen for some time wriggling about among the corpuscles; but the flagella of the human parasite are so small and so transparent, they are lost to view very quickly. The movement of the flagella goes on for a few minutes, as a rule about 5 minutes, but it may go on for a longer time.

Some of the crescents are converted into round bodies with pigment collected in the centre and a clear part outside but differing from those already described in that they do not give out flagella. These are said to be the female parasites. They often have two knobs at one side (D) it is not clear how these knobs are formed.

## Rosettes.

Rosettes are very seldom seen in the peripheral blood in Malignant Tertian cases. We have only seen two or three, although several hundreds of specimens of blood have been examined. In the case of Ramia, which will be given further on, a good rosette was found and 13 spores could be distinctly

counted. The rosette was at first about half the size of a blood corpuscle but it was left under the microscope for over an hour and then it had spread out and was as large as a red blood corpuscle.

In the blood of Malignant Tertian cases the forms of parasites that are seen usually are, first the Ring forms, then the Crescents, and after these the Flagellate bodies. When we come to examine the temperature charts it will be shown that the temperature chart can be divided into three fairly distinct periods, and it will further be shown that each of the three periods in the chart corresponds with the appearance of one of the three forms mentioned here. The primary fever with its chart showing a gradual slope downwards tallies in point of time with the presence of Ring forms; the interval of little or no fever tallies with the time when crescents are seen and the "Secondary fever" or flagellar fever tallies with the appearance of flagella.

# CHAPTER VIII.

## THE FLAGELLAR FEVER IN MALIGNANT TERTIAN.

Neither Manson nor Celli nor any of the authors that we have seen, describe or mention anything regarding the fever that occurs about the time that flagella are seen in Malignant Tertian cases.

Manson says in regard to Crescents that "the crescent body does not begin to show itself till it approaches maturity, about a week after the first crop of amœboid parasites associated with the paroxysm has appeared" and this we have verified in many cases, but as regards the exflagellation Manson says :—

> " In certain bloods exflagellation is easily procured; in others the opposite is the case. As regards the crescents, doubtless success depends in a measure on the degree of maturity of the parasite, young or effete crescents failing to evolve. There are other conditions affecting the process, however, which are as yet unknown."

The investigations which have been made here throw some new light on this point. While the investigations were being carried on a good many people (medical and non-medical) visited the Laboratory, and as we always tried to show them flagella we noticed that there was a certain stage when flagella could be found almost to a certainty. After the primary fever had disappeared there was an interval with low or only slight fever and then came a second rise of temperature,

and when this fever comes on flagella can be found. We have not failed to find flagella in the blood of any case that has been examined during this period. This fever to which we have given the name of "Secondary" or "Flagellar" fever does not always occur, but even when it does not occur a few flagella will be found if the blood is carefully examined. If the temperature be high, more flagella will be found; if it be low, less will be found; and if there be no fever, it may be difficult to find them. There is a distinct relationship between the amount of fever and the number of flagella to be seen, and therefore it would seem reasonable to consider that this fever is due to the flagella bodies, and if it is, we have next to consider whether the fever may in any way be connected with the process of exflagellation. Now it has apparently hitherto been supposed that exflagellation takes place only outside the body and after the blood has been drawn. There is no doubt that exflagellation is hastened by the withdrawal of blood from the body, but we have seen flagella bodies surrounded by phagocytes as soon as we could get the specimen under the microscope, and it is possible that the flagella may have been given out before the blood was drawn.

Manson speaking of the proneness to relapse in Malignant Tertian cases at page 66 says :—

> "After apparent recovery from the fever there is great proneness to relapse at more or less definite intervals of from 8 to 14 days."

It is important to distinguish between the Secondary fever or Flagellar fever, that has been described

above, and a Relapse. A relapse conveys the idea of a repetition of the process that occurs in the original fever. The relapse in Enteric and in Relapsing fever are apparently a repetition of the original process, but the Flagellar fever is quite different from the primary fever, for in the first place the Tertian nature of the fever is not so evident as it is in the primary fever, and there is more frequently a rise of temperature daily, though not always, while it lasts, and in the second place the examination of the blood shows that the parasites are in a very different condition from what they had been in the primary fever. In the primary fever we find the Ring forms, but in the Flagellar fever the Ring forms are only seen in small numbers if seen at all. Then another great point of distinction is that at the end of the primary fever we find crescents, whereas at the end of the secondary fever we find that the crescents have to a great extent if not entirely disappeared. The crescent appears to be something like a chrysalis stage during which the flagella are developed, in the same way as the legs and wings of a mosquito are developed during the time that it is coiled up in the form to which the name 'nympha' is applied. Now if the crescents are numerous at the beginning of the flagellar fever, and if they are in small numbers at the end of it; if the degree of fever tallies with the number of flagella bodies to be seen in the blood, and certainly in the cases that we have examined we have found that the higher the fever the larger the number of flagella that will be seen; if we find flagella bodies in freshly drawn blood, then it would seem to indicate a strong probability at least that the exflagellation

may occur in the blood before it is withdrawn from the human body, and to justify the introduction of the name which we have given to this particular stage of the fever, *viz.* the "Flagellar fever."

It is true as most authors say that we very rarely find exflagellated bodies in freshly drawn blood, but we have seen hundreds of times, how the phagocytes have a special antipathy to the flagella bodies, and how they come swooping down from a considerable distance to envelope and destroy the flagella body as soon as it begins to throw out flagella, so if the phagocyte can thus by some marvellous instinct (if the expression may be used in such a sense) lay hold of the flagella body when it is placed at a disadvantage, by being pressed under the cover glass how much more likely is it, that the phagocyte would be able to catch the flagella body when it is free in the blood ? If then the flagella body is captured by the phagocyte before the blood is drawn, this may account for the fact that we seldom see exflagellated bodies in freshly drawn blood.

It may be said that the phagocyte has a better opportunity of catching the flagella bodies when the blood is under the cover glass, because the latter cannot move so easily as the former when they are in this position. The force of this argument must be admitted, and although we are not prepared to assert positively that exflagellation does take place within the body still the arguments which have been given here, do seem to at least establish a probability that exflagellation may take place before the blood is

drawn. At any rate we think that it is a point which deserves further consideration. Relapses do however occur at irregular intervals afterwards and in these the Ring forms are again found.

It is with some hesitation that we have ventured to advance this view regarding the occurrence of exflagellation within the body, because it is opposed to the view which Manson and others apparently hold. Manson says :—

> " It is important to bear in mind that they are never seen in newly drawn blood, and that they come into view only after the slide has been mounted for some time—ten to thirty minutes, or even longer according to circumstances."

Manson's writings on Malaria are crammed full of facts,—facts so numerous that after some months of constant observations we are astonished not only by their accuracy but by their number, so in venturing to disagree with so high an authority on this point we do so with some hesitation.

In was on the 4th of January that one of the most intelligent of our observers Kya Thoung remarked that "you always find flagella in crescent cases when fever comes on." Since that time we have examined many cases in order to test the truth of this statement and we have found that there are three periods in a typical Malignant Tertian chart, and that each of these periods corresponds with a particular stage of the parasite.

There is first the primary fever which may be a *clear* Tertian—that is, with fever on alternate days

only—or with fever on the intervening days also. After the first day or two, each successive paroxysm is less than the preceding one so that if the highest temperatures are joined by a line, this line nearly always shows a "downward slope"—a marked contrast with untreated cases of Benign Tertian and Quartan.

*2nd period*:—After the "downward slope" comes an interval of a few days during which there is little or no fever, and then comes the

*3rd period*:—The Flagellar fever, which may have a Tertian appearance, but is not as "*clear*" a tertian as the primary fever as a rule, for we nearly always find some fever on the intervening days.

If we examine the parasites in these three stages we find in the

*1st period*:—Rings

*2nd period*:—a very marked diminution in the number of Ring forms, the Crescents gradually increasing, and at the end of it a few flagella bodies. In the

*3rd period* we find Ring forms very rare; crescents at first numerous and increasing, then decreasing and disappearing, almost if not entirely; flagella bodies increasing, decreasing, and finally disappearing.

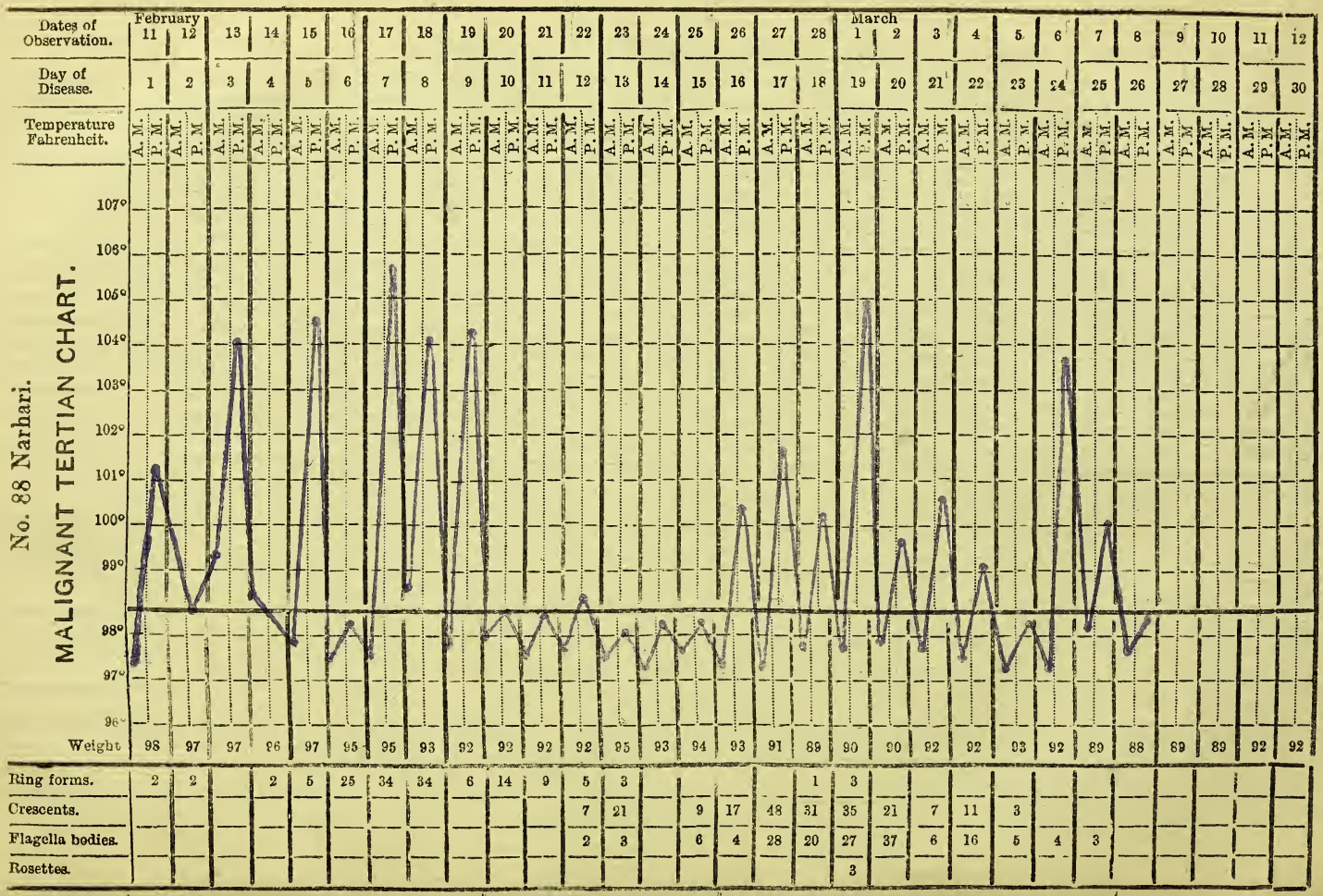
The primary fever is caused by the asexual sporulation of the Rosette forms; the interval occurs at the time when the Crescents are maturing; the secondary fever then comes on, and although it is contrary to the view held by Manson, Ross, Christy and others, still we believe that this part of the fever is caused by the breaking up of the crescents, or in other words that exflagellation does occur inside the body. We cannot

examine the blood before it is drawn and therefore we cannot *see* whether exflagellation does occur before the blood is drawn, but by examining the blood daily and noting the changes that occur we can draw inferences, and we would invite particular attention to the records of one case—the case of Narhari—and would ask whether any other reasonable explanation can be given for the alterations that occur, except the one which has been suggested here, *viz.*, that Ring forms change into Crescents, and that Crescents change into Flagella bodies before the blood is drawn.

In the table the results of the daily examinations are given, and in the chart the totals of the number of Rings, Crescents, &c. seen daily are entered. Allowance should be made for the fact that an equal length of time was not spent in examining the blood every day. The primary fever in this case is not typical for it does not show the downward slope.

The chart has been divided into three periods corresponding to the primary fever, the crescent forming interval, and the Flagellar fever. If we further subdivide the third period into three subperiods and then count the numbers of the different kinds of parasite seen in each period or subperiod we shall find the totals as follows :—

| Form of Parasites. | 1st | 2nd | 3rd | | |
|---|---|---|---|---|---|
| | *a* | *a* | *a* | *b* | *c* |
| Ring forms ... | 110 | 31 | 4 | 0 | 0 |
| Crescents ... | 0 | 37 | 131 | 39 | 3 |
| Flagella bodies ... | 0 | 11 | 79 | 59 | 12 |


No. 88 Narhari.
MALIGNANT TERTIAN CHART.
Dates of Observation.
February
March
Day of Disease.
Temperature Fahrenheit.
A. M.
P. M.
107°
106°
105°
104°
103°
102°
101°
100°
99°
98°
97°
96°
Weight
98 97 97 96 97 95 95 93 92 92 92 92 95 93 94 93 91 89 90 90 92 92 93 92 89 88 89 89 92 92
Ring forms.
2 2 2 5 25 34 34 6 14 9 5 3 1 3
Crescents.
7 21 9 17 48 31 35 21 7 11 3
Flagella bodies.
2 3 6 4 28 20 27 37 6 16 5 4 3
Rosettes.
3
Primary fever.
Crescent forming interval.
Flagellar fever.

# No. 88 Narhari.

| Date. | Number of specimen. | Hour when blood drawn. | Temperature. | Ring forms. | Rosettes. | Crescents. | Flagella bodies. |
|---|---|---|---|---|---|---|---|
| 16-2-01 | 1 | 12-30 p. m. | 95·0 | 25 | ... | ... | ... |
| 17-2-01 | 1 | 4-30 p. m. | 105·8 | 14 | ... | ... | ... |
| | 2 | 4-36 | 105·8 | 2 | ... | ... | ... |
| | 3 | 5-10 | 105·0 | 4 | ... | ... | ... |
| | 4 | 6-10 | 104·0 | 3 | ... | ... | ... |
| | 5 | 6-40 | 103·4 | 8 | ... | ... | ... |
| | 6 | 7-11 | 103·4 | 3 | ... | ... | ... |
| | | | | **34** | .. | ... | ... |
| 18-2-01 | 1 | 9-15 a. m. | 97·6 | 5 | ... | ... | ... |
| | 2 | 9-45 | 97·0 | 2 | ... | ... | ... |
| | 3 | 10-40 | 97·2 | 3 | ... | ... | ... |
| | 4 | 11-20 | 97·6 | 2 | ... | ... | ... |
| | 5 | 12-15 p. m. | 97·4 | 4 | ... | ... | ... |
| | 6 | 1-0 | 96·0 | 3 | ... | ... | ... |
| | 7 | 2-20 | 97·4 | 6 | ... | ... | ... |
| | 8 | 3-15 | 97·8 | 9 | ... | ... | ... |
| | | | | **34** | ... | ... | ... |
| 19-2-01 | 1 | 10-30 a. m. | 97·6 | | ... | ... | ... |
| | 2 | 11-10 | 98·6 | 1 | ... | ... | ... |
| | 3 | 4-30 p. m. | 103·6 | 5 | ... | ... | ... |
| | 4 | 4-50 | 103·6 | | ... | ... | ... |
| | | | | **6** | ... | ... | ... |
| 20-2-01 | 1 | 9-45 a. m. | 98·2 | 3 | ... | ... | ... |
| | 2 | 2- 5 p. m. | 97·6 | 7 | ... | ... | ... |
| | 3 | 4-20 | 98 0 | 4 | ... | ... | ... |
| | | | | **14** | .. | ... | ... |
| 21-2-01 | 1 | 11-50 a. m. | 97·8 | 4 | ... | ... | ... |
| | 2 | 2-15 p. m. | 97·2 | 2 | ... | ... | ... |
| | 3 | 2-40 | 97·4 | 3 | ... | ... | ... |
| | | | | **9** | ... | ... | ... |
| 22-2-01 | 1 | 9-10 a. m. | 98·0 | 4 | ... | ... | ... |
| | 2 | 12 | 97·6 | 1 | ... | 3 | 1 |
| | 3 | 6 p. m. | 97·6 | | ... | 4 | 1 |
| | | | | **5** | ... | **7** | **2** |
| 23-2-01 | 1 | 8-10 a. m. | 97·6 | ... | ... | 5 | 3 |
| | 2 | 12-35 p. m. | 97·4 | ... | ... | 6 | ... |
| | 3 | 4-35 | 97·6 | 3 | ... | 10 | ... |
| | | | | **3** | ... | **21** | **3** |
| 25-2-01 | 1 | 4 p. m. | 97·6 | ... | ... | 2 | 3 |
| | 2 | 5 30 | 97·4 | ... | ... | 7 | 3 |
| | | | | ... | ... | **9** | **6** |

| Date. | Number of specimen. | Hour when blood drawn. | Temperature. | Ring forms. | Rosettes. | Crescents. | Flagella |
|---|---|---|---|---|---|---|---|
| 26-2-01 | 1 | 8-8 a. m. | 97·6 | ... | ... | 5 | |
| | 2 | 9-30 | 97·0 | ... | .. | 12 | .. |
| | | | | ... | ... | **17** | **4** |
| 27-2-01 | 1 | 11 a. m. | 98· | ... | ... | 8 | |
| | 2 | 12-20 p. m. | 99· | ... | ... | 23 | 1 |
| | 3 | 2-25 | 101·6 | ... | ... | 17 | |
| | | | | ... | .. | **48** | **2** |
| 28-2-01 | 1 | 9 a. m. | 97·4 | ... | ... | 13 | |
| | 2 | 11-45 | 97·0 | 1 | ... | 18 | 1 |
| | | | | **1** | ... | **31** | **2** |
| 1-3-01 | 1 | 8-30 a. m. | 98·2 | ... | ... | 10 | |
| | 2 | 12-35 p. m. | 99·8 | 1 | 1 | 11 | |
| | 3 | 1-15 | 101·0 | 2 | ... | 6 | |
| | 4 | 3-20 | 104·2 | ... | 2 | 8 | 1 |
| | | | | **3** | **3** | **35** | **2** |
| 2-3-01 | 1 | 8-20 a. m. | 98·2 | ... | ... | 5 | 1 |
| | 2 | 10 | 97·4 | ... | ... | 9 | 1 |
| | 3 | 2-15 p. m. | 97·8 | ... | ... | 7 | |
| | | | | ... | ... | **21** | **3** |
| 3-3-01 | 1 | 9 a. m. | 97·6 | ... | ... | **7** | |
| 4-3-01 | 1 | 7-30 a. m. | 99· | ... | ... | 5 | |
| | 2 | 1 p. m. | 97·6 | ... | ... | 6 | |
| | | | | ... | .. | **11** | |
| 5-3-01 | 1 | 9 a. m. | 97·6 | ... | ... | 3 | |
| 6-3-01 | 1 | 8-30 a. m. | 98·8 | ... | ... | ... | |
| 7-3-01 | 1 | 12 a. m. | 100· | ... | ... | ... | |
| 9-3-01 | 1 | 12-26 p. m. | 97·6 | ... | ... | 3 | |
| 10-3-01 | 1 | 11 a. m. | 98·0 | ... | . | 2 | |
| 11-3-01 | 1 | 7-20 a. m. | 97· | ... | . | 3 | |
| 12-3-01 | 1 | 11-30 a. m. | 97· | ... | | 3 | 2 |
| 13-3-01 | 1 | 8. a. m. | 97·2 | ... | ... | 2 | 1 |

Duration of each examination 20 minutes.

There were no crescents or flagella bodies in the first period, although 110 Ring forms were found. Crescents appear in the second period and a few flagella bodies, but most of these were seen on the evening before the Flagellar fever came on.

It is the third period to which special attention is invited. Note how the crescents soon begin to diminish in number and note how in the first subperiod the crescents are nearly double the number of the flagella bodies, while in the second subperiod the flagella bodies outnumber the crescents, and in the third subperiod the flagella bodies are 4 times as numerous as the crescents.

The crescents disappear—there will be a few remaining as there will be a few green stalks in a field of ripe corn—the flagella bodies also disappear,—but notice how the numbers in respect to each other alter,—the Crescents being at first in the majority, the flagella bodies being afterwards in the majority. Can any other reasonable explanation be offered to account for this change in numbers except the one which has been put forward now, *viz.*, that the Crescents have been converted into flagella bodies before the blood had been drawn ?

A phagocyte never attacks a Crescent, and if the Crescent is not converted into a Flagella body where does it disappear to and how is it disposed of ? A phagocyte attacks a flagella body in the most marvellous way, and can we believe that a cell which performs a function of this kind when the blood has been drawn has not got a similar function to perform while it is still within the body ?

If we examine the record we find on the evening of the 1st March and the morning of the 2nd March that the number of flagella bodies was 12 plus 16, and the number of crescents seen in the same slides was 8 plus 5, so that 28 flagella bodies were seen while 13 crescents were counted. Up to the 1st March the crescents outnumbered the flagella bodies. We think it is a fair inference to draw that exflagellation was at its maximum on the evening or night of the 1st March. What was the temperature on that evening? It was the highest during this part of the fever and why? Was it due to the breaking up of Rosettes and the invasion of blood corpuscles by the spores? Or was it due to the exflagellation.

It is true that a small number of Rosettes and Ring forms were seen, but as we said above you always find a few green stalks in a ripe field of corn; it is also true that 150 flagella bodies were counted in the third stage while only 4 Ring forms were found, and that 110 Ring forms were found in the Primary fever and not one flagella body was found. If the Secondary fever was not due to some different process from that which took place in the Primary fever, how can the alteration in the condition of the parasites which were observed be explained?

Had the statement, that exflagellation takes place only after the blood has been drawn, not been made by many high authorities, we think that the observations recorded above would carry conviction that exflagellation does take place inside the human body, but further evidence in favour of this view can be given from observations which have been made on sparrows' blood and also from the records of observations which have been made by Stephens and Christophers in Lagos on the West Coast of Africa, but these will be considered later.

# CHAPTER IX.

## MALIGNANT TERTIAN CHARTS.

Quartan charts and Benign Tertian charts can be easily placed in groups for the purposes of description, but when we attempt to classify the Malignant Tertian charts we are met with some difficulties for they present great variety. There are some that might be called clear Tertians, that is, with fever on one day and no fever on the next, and there are others in which we find fever every day but with fever a little higher on alternate days. We propose however to follow a different system of classification, but at the outset we must make it clear that the different groups do not represent any inherent differences in the parasites but rather different degrees of severity or different stages in the fever.

We have said that the Malignant Tertian chart often shows the following stages :—(1) the downward slope, (2) the crescent forming interval, (3) the flagellar fever period. All charts do not however show these three periods, for some only show the downward slope, and there are some which show only the secondary fever, that is, in the case of men who did not come to Hospital when they were first attacked. Then there are some which show a relapse or a fresh onset of fever coming some time after the Flagellar fever. We propose then to illustrate the Malignant Tertian fever by giving

(1) Charts showing the downward slope only.

(2) Charts showing the downward slope, the crescent forming interval and the Flagellar fever.

(3) Charts showing the Flagellar fever at the time of admission.

(4) Charts showing a relapse.

(5) Irregular cases.

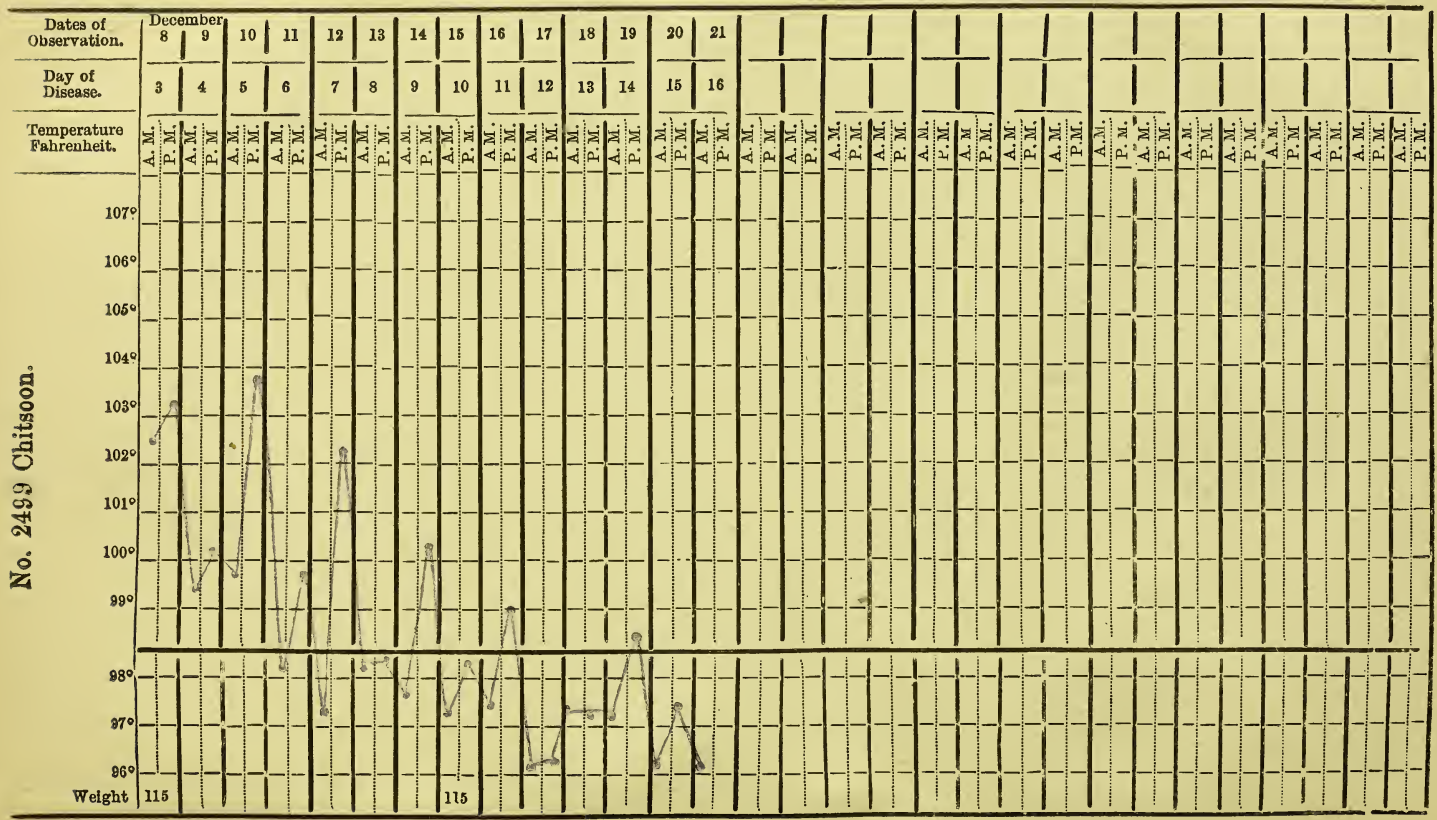
The number of cases that have been thus classified is 46. It may be said that it is not advisable to draw definite conclusions from such a small number, but as quinine has not been given to these cases for some time after their admission, and as it would not be advisable to withold quinine from a large number, the natural course of the fever can perhaps best be studied from observations that have been made on small numbers. It ought however to be mentioned that these cases were observed in the winter months, and at this season malarial fevers are much milder on the whole than those which are met with in the months of September and October.

Cases to illustrate the Downward Slope :—

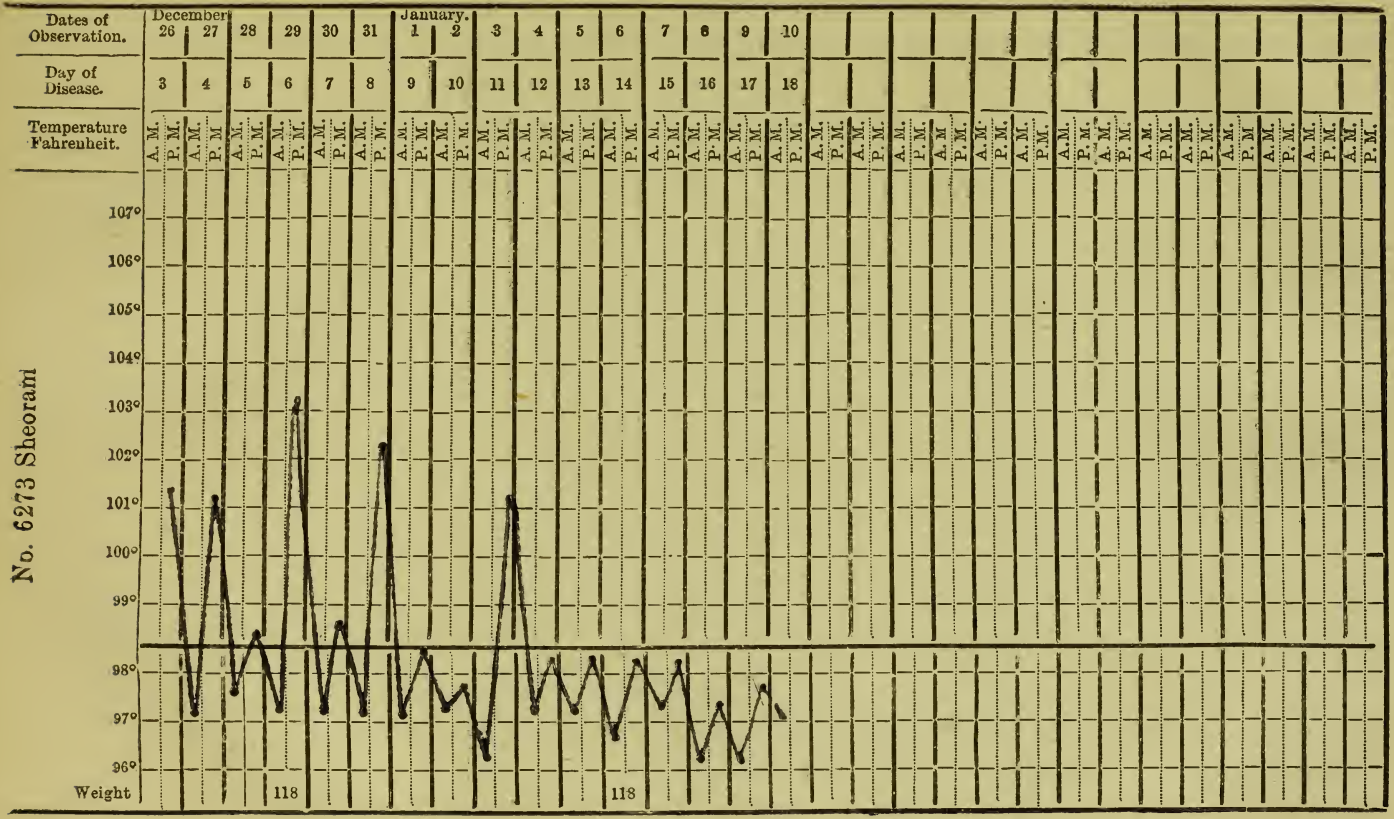
*1st, No.* 2499 *Chitsoon.*—This chart shows the higher temperatures on the 8th, 10th, 12th, &c., and it also shows a slight rise of temperature in the intervening days at first. It shows also that the temperature does not fall to the normal in the intervening days. Celli remarks at page 46 :—

> "This form of Tertian is also called Malignant inasmuch as it may become malignant, the paroxysms being prolonged and approaching one another till it simulates a continued fever and become subcontinued."

# MALIGNANT TERTIAN CHART.

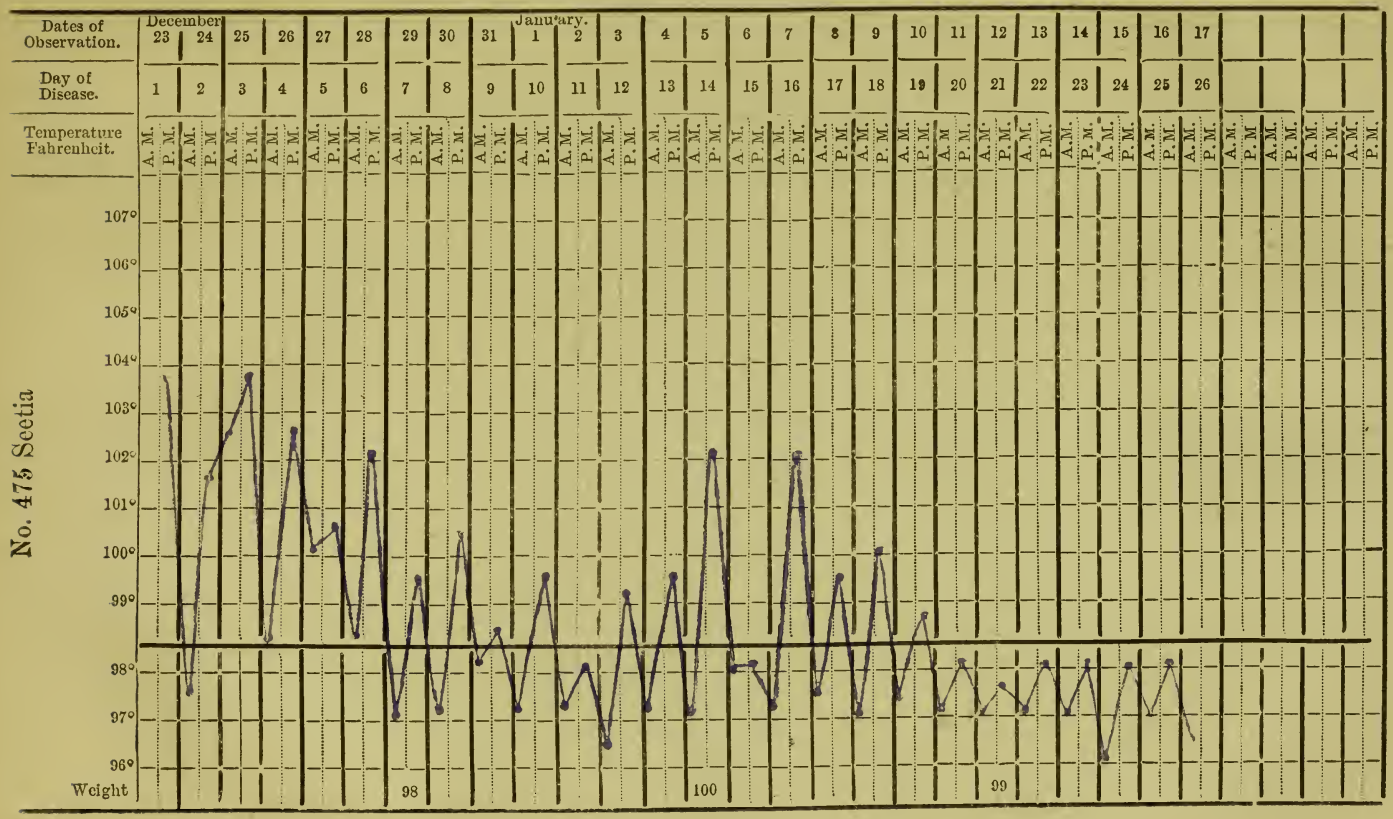


# MALIGNANT TERTIAN CHART.




No. 6273 Sheoraini

# MALIGNANT TERTIAN CHART.




No. 475 Scotia

Celli further remarks that "it is also called aestivo-autumnal tertian, because it is observed only in the summer and autumn, never in the spring." By far the larger number of cases of fever admitted into this Hospital during the months of January and February were of the Malignant Tertian variety so the name aestivo-autumnal should be used with a certain amount of reservation.

On the 18th of December, that is, eleven days after admission to Hospital, and on the 13th day of the disease, 12 crescents were seen in one slide in a few minutes. On the 26th December only one crescent was found. On the 9th January nothing was found. Manson (page 16) says "the crescent body does not begin to show itself till it approaches maturity, about a week after the first crop of amoeboid parasites associated with the fever paroxysm has appeared."

The next chart which is taken to show the gradual slope of temperature is that of Sheoram. Crescents were found on the 15th. His blood had not been examined however for a week so it is probable that crescents appeared earlier.

The next group of charts shows the gradual slope downwards, an interval of slight or no fever, and then the secondary fever. To illustrate this group we may take first the chart of Seetia. Note the apparent change of day of the fever. At first it came on the 23rd and 25th, then it began to come on the even days 26th, 28th, &c.

On the 4th January, the 13th day of the fever, about a dozen crescents were seen, and on the same

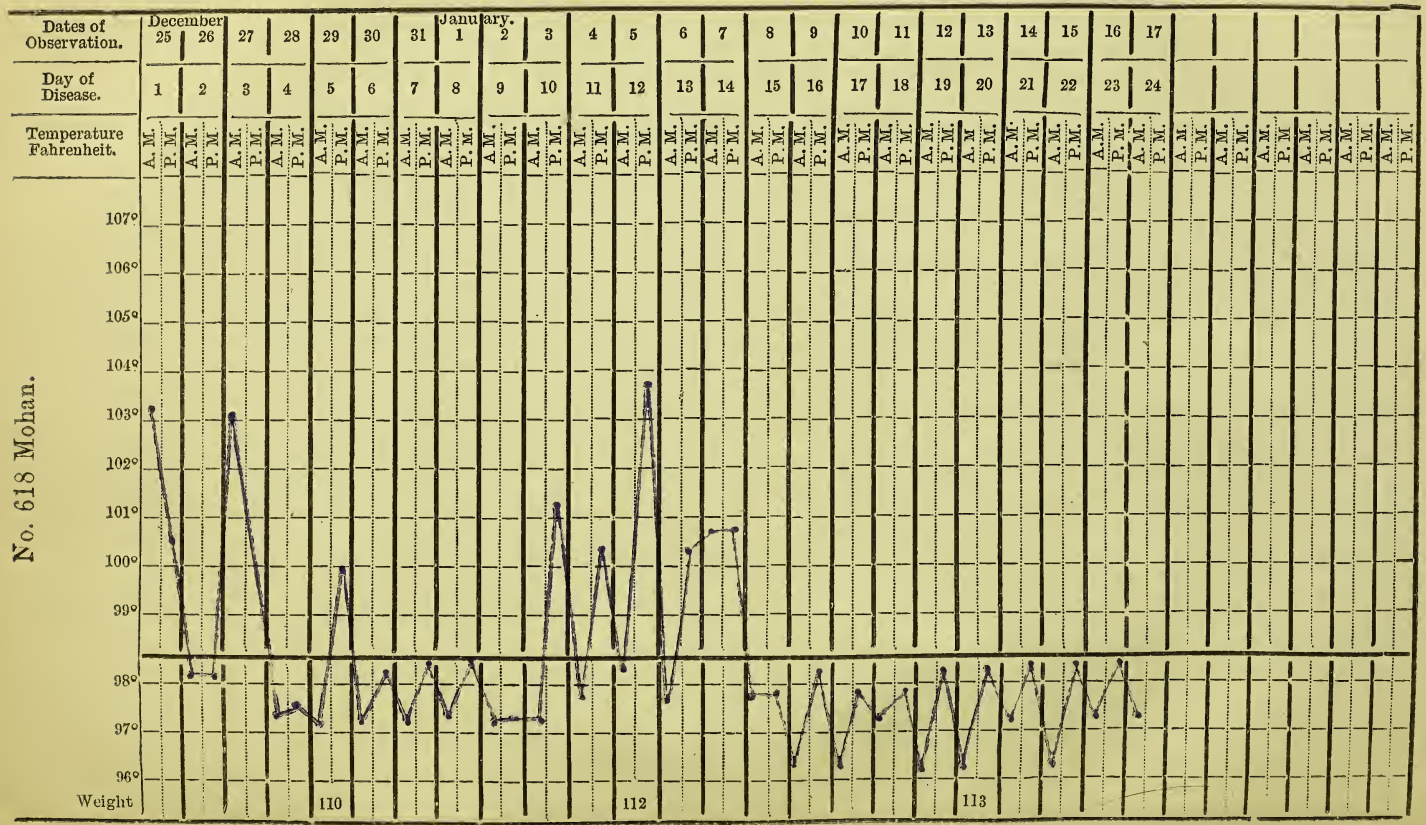
day flagella bodies were seen. The secondary fever lasts for about a week; it is irregular but presents some appearance of tertian.

On the 13th January, that is the 22nd day of the disease, nothing was found in the blood. This is the usual course, for crescents are not found in large numbers after the secondary fever disappears. Now if this fever which we have called the Secondary fever were a relapse then we should expect to get crescents after it as we do after the primary fever. But in some dozens of cases we find the same sequence of events—the gradual slope, the interval of no fever or of little fever when many crescents are found, the secondary fever in which flagella are seen, and then the disappearance of fever, while at the same time the crescents and flagella disappear from the blood, at least from the peripheral blood.

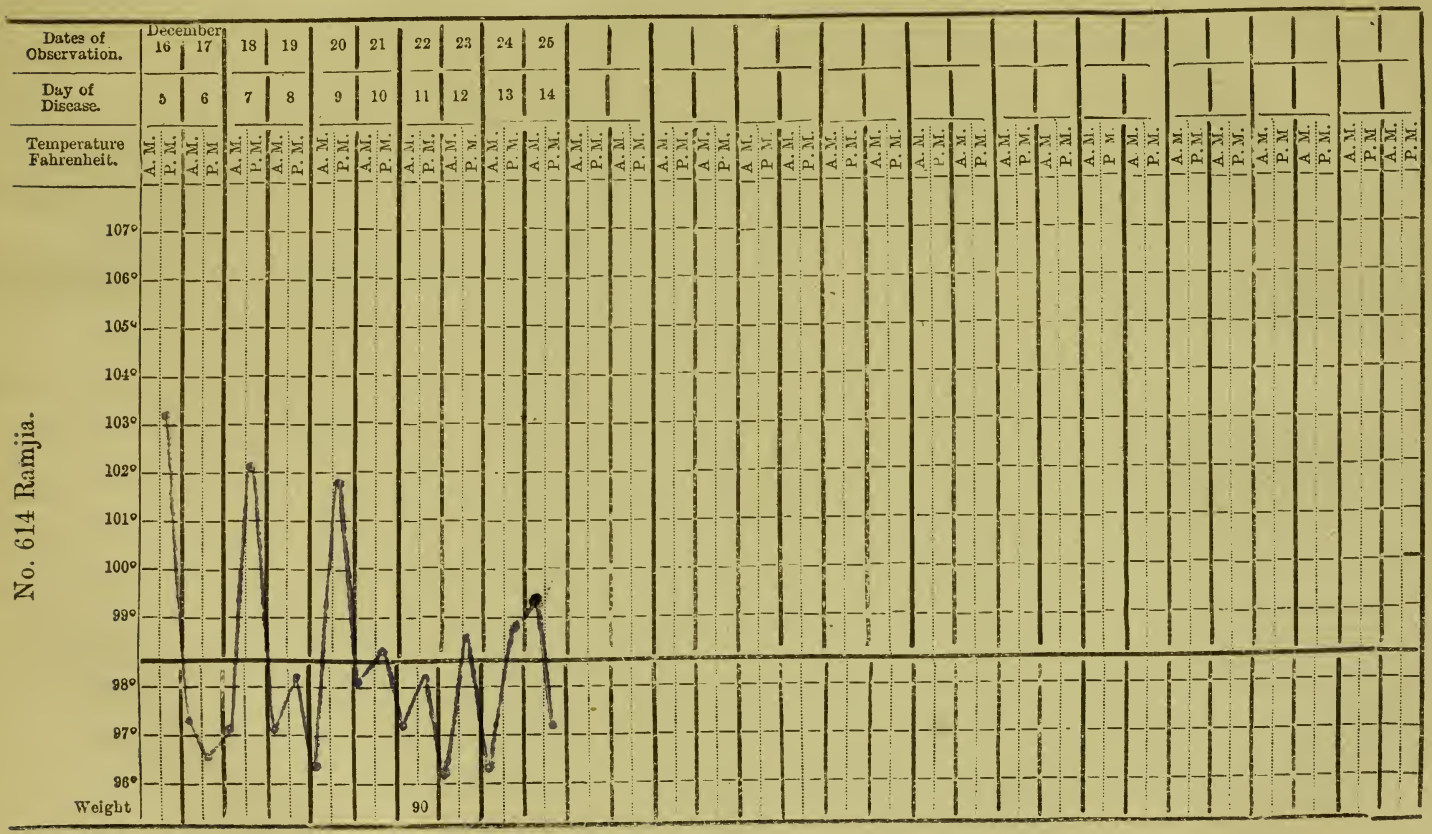
At first we were not able to prove that the Malignant Tertian parasite can be conveyed by the anopheles, and we thought that this might be due to the fact that care had not been taken to allow the mosquitoes to bite when the Flagella bodies were present. Experiments were then made with mosquitoes which were allowed to bite a man during the Flagellar period. These will be described later.

*Case IV Mohan.*—This chart illustrates the downward slope, the crescent interval and the Flagellar fever. On the eighth day 2 crescents were seen. On the 10th day many crescents and flagella bodies were seen. On the 11th day flagella were seen. On the 26th day, although he had no fever, his blood was examined as discharged crescent cases were from time

# MALIGNANT TERTIAN CHART.



# MALIGNANT TERTIAN CHART.



to time examined. Colonel Poynder, I. M. S., happened to be here at the time and he made the following note in regard to the flagella body :—

> "Cell full of actively moving grains of pigment with a clear space externally ; shortly some of the grains of pigment moved out into the clear space having developed flagella and whisked about actively. A short distance away in the field was a phagocyte which suddenly swooped down on the scene of action—rapidly enveloping the whole cell and the moving flagella. Within a few moments, movement had stopped and the pigment gradually became smaller and the phagocyte more finely granular in appearance."

On the 23rd January, Mohan had fever and ring forms were seen again.

Where did these Ring forms come from? Have they passed through the flagella stage? that is, are they the result of the union of the male and female in the blood *in the body?*

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## Malignant Tertian Charts—Group III.

The next group of charts are chosen to indicate the Flagellar fever at the time of admission to Hospital. Some of these cases had been in Hospital previously, and some may have had slight fever without coming to Hospital for treatment. This group is a purely artificial group for they do not represent a different kind of fever, but by putting them in a separate group we wish to draw attention to the importance of recognizing the Flagellar fever. For instance the first chart given here is that of *Ramjia.* He had been

in Hospital from the 3rd till the 11th of December and he had been discharged before the time when we had discovered the Flagellar fever. He came back to Hospital on the 16th of December and the chart given here shows particulars of his case after that date.

16th—(that is the date of second admission) crescents were found in his blood.

17th—Many crescents and some flagella seen by Dr. Agnes Henderson.

19th—12 crescents seen in about two minutes. 4 crescents seen in one field : flagella also seen.

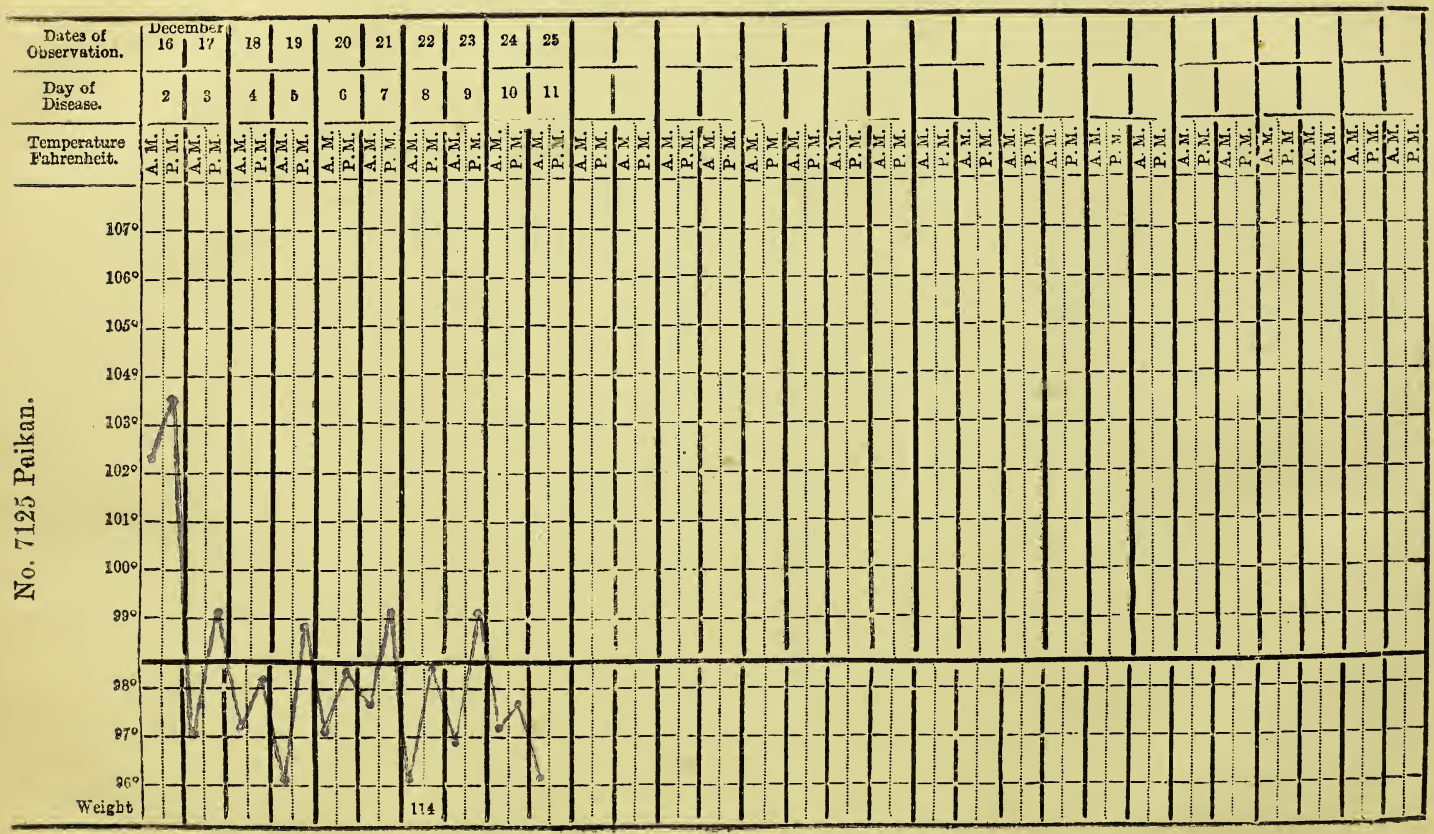
25th —discharged from Hospital.

26th—4 crescents seen in 10 minutes examination.

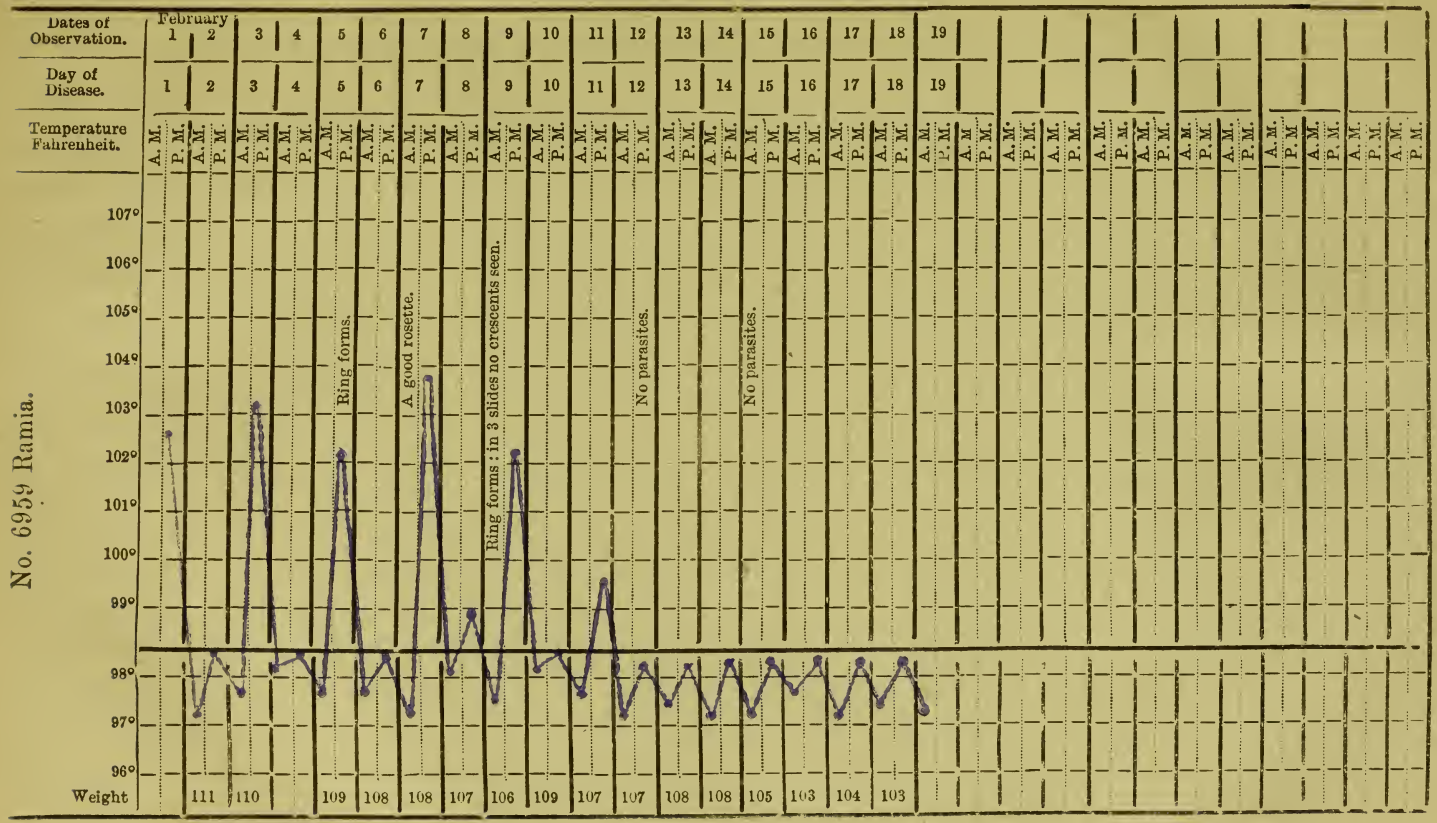
This case illustrates the importance of the recognition of the Flagellar fever, for the man was discharged from Hospital before the onset of this fever and he had to come back to Hospital again. We may be asked to say whether an officer who wishes to go on tour in his district can safely go after he has apparently recovered from an attack of fever. If he had been suffering from a Quartan it would be perfectly safe to give permission to go, but if the fever from which he had recovered were the primary part of a Malignant Tertian, then it would be clearly advisable to say no.

*Case VI, Malignant Tertian.*—Paikan had not been in Hospital before, but he said he had had fever 6 days before he came to Hospital. On the day of admission his temperature was over 103. Many speci-

# MALIGNANT TERTIAN CHART.



# MALIGNANT TERTIAN CHART.




No. 6959 Ramia.

mens of his blood were examined on this day and many flagella bodies were seen but only one crescent was found.

19th—One crescent seen after a long search; Phagocytes have much pigment; Flagellar bodies seen.

26th—No crescents seen in 5 minutes search.

The history of previous fever, the finding of flagella and crescents on the day of admission, and the absence of crescents at the end of the fever show clearly that the man was admitted when he was suffering from the Flagellar fever.

Two crescents were found on the 9th January.

### Malignant Tertian—Group IV.

The chart of Ramia will be given to illustrate the fact that in Malignant Tertians we sometimes have a chart which presents a clear Tertian appearance resembling in appearance the chart of a Benign Tertian.

### Malignant Tertian—Group V.

It might be expected that we ought to be able to dispose of all the charts in the groups that have been already described, but unfortunately this is not the case. There are some charts which show an attack of fever coming several weeks after the first attack and these present such a great variety that it would be impossible to make them fit into any typical group.

# CHAPTER X.

## AN ATTEMPT TO RECONCILE THE VARIOUS VIEWS REGARDING MALIGNANT TERTIAN FEVER.

The literature on Malignant Tertian fever is rather confusing, for we find authors making statements which are widely at variance. It may be useful to consider whether a knowledge of the fact that there are more or less definite periods during which particular forms of parasites are seen, will help us to reconcile what appear to be directly contradictory statements. Some extracts from the writings of various authors will be given below in order to show to what extent they differ. Special prominence will be given to the views of Drs. Stephens and Christophers who have recently written a Report on "The Malarial Infection of Native Children" in Lagos on the West Coast of Africa, because it would seem that their observations to a large extent substantiate what we have observed here and because the conclusions which they have drawn and the theories they have advanced do not appear to be justified by the observations they have recorded. Their paper is published in the Royal Society's "Reports to the Malarial Committee" third series. Unfortunately in the tables which are published with their paper they do not make any distinction between the crescent and the flagella bodies but classify them all together under the heading "gametes," and they do not give charts of the cases nor mention the temperatures of those in which "*gametes*" were found, nor say whether there was any difference in the temperatures

when flagella bodies were found. But they do mention at page 9 that "contrary to our expectation there is a sequence in the occurrence of parasites." Now every body knows, and Manson and Celli have distinctly pointed out, that there is a *sequence* from Ring forms to Crescents, and Stephens and Christophers were evidently aware of this for they say in an earlier part of their paper "While in European blood, subsequent to an attack of fever it is the crescentic form of the gamete that is encountered &c." What they evidently meant to convey is that there is an "alternation" for they quote cases to show that they sometimes found asexual parasites, followed by gametes, and others in which they found gametes followed by asexual forms. The cases that we have met with here have been divided into 5 groups, *viz.*—

(1) Those showing the Primary fever without Flagellar fever.

(2) Those showing the Primary fever and the Flagellar fever.

(3) Those showing the Flagellar fever only—they are cases that had not come to Hospital during the primary fever.

(4) Those showing true relapses, that is, cases showing the primary fever, the Flagellar fever, and afterwards a true relapse in which ring forms are again found.

(5) Irregular cases in which many ring forms and Flagella bodies are found at the same time.

The cases recorded by Stephens and Christophers in their Tables would fit into these groups fairly well.

For instance their case 9 : many parasites in the 2nd half of July : only one gamete seen in August (10th) would probably fit in with our group I ; their case No. VII of Table II showing 5 asexual parasites on the 4th of August and 7 gametes on the 12th August would probably fit in with our group IV.

Of course, as said above, they have not given the temperature charts and they have not made any distinction between the crescents and flagella bodies in their Tables, but the results of the blood examinations show such a strong resemblance to those which we have found here that it would seem as if there is a great similarity between the Malignant Tertian of Lagos and the Malignant Tertian which we find here.

When we come to consider the question whether the Crescent changes into the Flagella body before the blood is drawn from the body we find the opinions of writers as follows:—

Manson at page 13 says:—

> " It is of importance to bear in mind that they (flagellated bodies) are never seen in newly drawn blood and that they come into view only after the slide has been mounted for some time—10 to 30 minutes."

Ross—West African Report says: "they remain unchanged within the vertebrate hosts."

Christy—page 3 : "the fact that the flagellated body did not come into existence until the blood left the vessels and was outside the human body &c."

Celli—page 48 : "In the human body they (crescents) appeared to be and in fact are sterile."

Manson is of opinion that Flagella bodies are never seen in freshly drawn blood and the authors mentioned above agree with him.

Stephens and Christophers however at page 5 of the Report mentioned above say :—

> " It is here that Native blood presents many points of divergence from European blood—features that have hitherto not been recorded. While in European blood subsequent to an attack of fever it is the crescentic form of the gamete that is encountered, in Native blood while gametes are exceedingly common, yet the crescentic form is rare, the gametes assuming the spherical forms found in simple tertians and quartans ..... .....We are convinced on the contrary that the crescentic form is not an essential distinctive feature of the æstivo-autumnal parasite."

Stephens and Christophers having found what Manson, Ross and Celli say never occurs, proceed to give an explanation. Now there are two ways in which the difference in the observations might be explained—one that Native blood is different from European blood, the other that the specimens of blood may have been examined at different periods of the disease. Stephens and Christophers do not apparently take the latter into consideration ; without bringing forward any argument, or assigning any reason for the conclusion they have drawn, they say that there are many points of divergence between Native and European blood, and they do not make the suggestion that the difference in the observations may possibly be accounted for by the observations having been made at different stages of the attack.

We have seen a good many cases of malaria in Natives of India and in Europeans and the symptoms seem to be exactly the same in both, and as far as we can judge from the descriptions given of the parasites by Manson and Celli the parasites seen here and those seen in other parts of the world seem to be the same, excepting in some minor points which may possibly be due to differences in description We have seen however that there is a period when more crescents are found than flagella bodies and there is a period when the flagella bodies are more numerous than the crescents, and until Stephens and Christophers have examined a number of cases throughout their whole course we must hesitate to accept their statement, that the crescent does not occur in the æstivo-autumnal fever.

The next question to consider is whether there is any connexion between the crescent body or flagella body and relapses, and we may take relapse here to include secondary fever from whatever cause.

Manson (page 66) says "the crescent body does not cause fever." Celli page 52 says "so that Golgi erroneously believed that these crescents represented the germ of recurrent fevers." Stephens and Christophers page 9: "We cannot in the present state of our knowledge, attribute any part to the gametes in the production of relapses"; but in the same page and a few lines above these writers say :—

> "So that it would appear as if there was a succession of gametes, in the same way as we have a succession of developments of asexual parasites leading to the ordinary febrile attacks of Europeans."

What is meant by this last paragraph is not clear. Do they believe that one gamete (crescent) produces another gamete without going through the regular stages of ring form, crescent, flagellate body ? If so, they do not bring forward any arguments to support this view.

They have been puzzled by what they have seen, but it is perfectly clear that they have been examining cases during the flagellar fever period.

We believe then that we have shown that many of the differences of opinion which exist at present will disappear when it is recognised that there are two fever periods in the Malignant Tertian and if writers on the subject will take care to particularise what period of the fever they are describing.

In Manson at page 66 we find :—

> "A Plehn states that during a period of two years' residence in Africa he only once saw the flagellated body."

And is it not curious that Stephens and Christophers should have found it so frequently?

# CHAPTER XI.

## MALARIA IN SPARROWS.

Two kinds of parasite have been found in sparrows, one called the proteosoma which is round in shape and the other halteridium because it was supposed to resemble a halter. In the investigations which have been made here it has been found that those sparrows which have the proteosoma in their blood get a rise of temperature every other day or Tertian fever, and those which have the halteridium in their blood get a rise of temperature every third day or Quartan fever.

The observations which led to the discovery of the fact that sparrows get Tertian and Quartan fever were made during the months of March, April, May, June, July and August, and during these months there were a few admissions of men to Hospital for Tertian and Quartan fevers. This seemed rather curious, and the question was asked whether the parasites which cause Quartan in sparrows are the same as those which cause Quartan in man, and are the Tertian parasites of sparrows the same as the Tertian parasites of man. If there is any truth in the statement which is now accepted by many writers on Malaria in regard to the conveyance of malarial parasites from man to man by means of mosquitoes then it would be important to enquire whether parasites might be conveyed from birds to man.

In the Lecture on Malaria which Professor Koch delivered at Eastbourne on the 26th July of the present year he said, when speaking of the measure proposed by him for extermining malaria, that " in making this

"proposal I presuppose two things—firstly, that the "malaria parasites are restricted to man—As to the first "of these proposals I regard it as adequately proved "by the fact that nobody has yet succeeded in finding "parasites identical with the human malaria parasite in "the blood of any animal."

A few days before Koch had delivered this Lecture, he had in his Lecture at the Tuberculosis Congress given his reasons for thinking that the bacillus of bovine tuberculosis was not the same as the bacillus of human tuberculosis. It is well known that bacilli alter in many respects according to their environment, and as it is now looked on as a matter of the very greatest importance to decide whether the tubercle of man is the same as the tubercle of cattle, so from the point of view of prevention it is also important to enquire whether the malarial germ of man is the same or is in any way related to that of animals or birds.

Koch presupposes that the malarial parasites of man are restricted to man, and he bases his principal method of prevention on this assumption. The malarial parasites of the sparrow differ considerably in appearance from those of man, but this might be expected from the fact that the blood of birds differs so much from that of man. Are the differences which have been observed between the human and bird parasites due to environment merely or are the parasites totally different? It was with a view to throwing some light on this subject that the investigations regarding sparrow malaria have been made.

Altogether 292 sparrows were examined. Their temperatures were taken twice daily and entered in charts. Each blood examination lasted 5 minutes and

the number and kind of parasites found were entered in the charts. The effect of quinine given by mouth as well as hypodermically was watched in some cases and the effect of methylene blue in others. In the table given below is shown the number of sparrows examined in each month, the number in which Quartan parasites were found, the number in which Tertian parasites were found, the number with both kinds of parasite, and the number in which no parasites were found. The percentage of the whole number in which parasites were found is also noted.

*Table showing the number of sparrows examined.*

| Month. | | Quartan. | Tertian. | Double infection. | No. of sparrows without parasites. | Total. | Percentage in which parasites found. |
|---|---|---|---|---|---|---|---|
| March | 1901 | 4 | 10 | 13 | 7 | 34 | 79 |
| April | „ | 26 | 22 | 2 | 17 | 67 | 75 |
| May | „ | 17 | 6 | 0 | 71 | 94 | 24 |
| June | „ | 10 | 1 | 1 | 32 | 44 | 27 |
| July | „ | 18 | 0 | 0 | 5 | 23 | 78 |
| August | „ | 26 | 0 | 0 | 4 | 30 | 87 |
| | | 101 | 39 | 16 | 136 | 292 | |

This table shows that the percentage of sparrows having parasites in their blood in March and April was 75, and in the two following months it was about 25. In the months of May and June malarial fevers in man are at their minimum, and it is worthy of notice that the numbers of sparrows infected in these two months appears to be less.

Second, it is also worthy of notice that the proportion of Tertian parasites found in May and June decreased considerably, and this would suggest the possibility that the agency by which the Tertian is conveyed to birds may differ from that by which the Quartan is conveyed. In the experiments which were made here regarding human malaria we were not able after many experiments to convey Quartan from man to man by means of anopheles although there was evidence in favour of the Benign tertian having thus been conveyed.

Third, Dr. Lawrie of Hyderabad fame, has written in the *Indian Medical Gazette* regarding sparrow malaria, and he has made a number of statements which we have over and over again proved to be wrong, such as that the halteridium and the proteosoma are the same and that the parasites are not affected by quinine. Dr. Lawrie's paper will be dealt with separately, but it has occurred to us that if he was examining the sparrows at a time when the Tertian parasites are not found, then it would be easy to understand how he made such a great mistake in saying that sparrow parasites are not affected by quinine. The Tertian parasite is undoubtedly affected by quinine, but the Quartan is only slightly affected by it.

While carrying out these observations we noticed that those sparrows which had the long parasite (halteridium) in their blood had higher temperatures every third day, that is, they had Quartan fever. This was noticed in nearly every case—101 altogether. The temperatures of some of these sparrows were taken for as many as 60 days and throughout the whole time the chart showed the Quartan appearance. Similarly most of the 39 with the round parasites showed a Tertian appearance in the charts, and those in which no parasites were found never showed either a Quartan nor a Tertian appearance in their charts. After the administration of quinine to those which had the Tertian parasites the Tertian appearance of chart disappeared if the quinine was given in sufficiently large doses, affording good evidence that the fever was due to these parasites.

In 16 both the Tertian and Quartan parasites were found together and in these the fever was as a rule somewhat irregular.

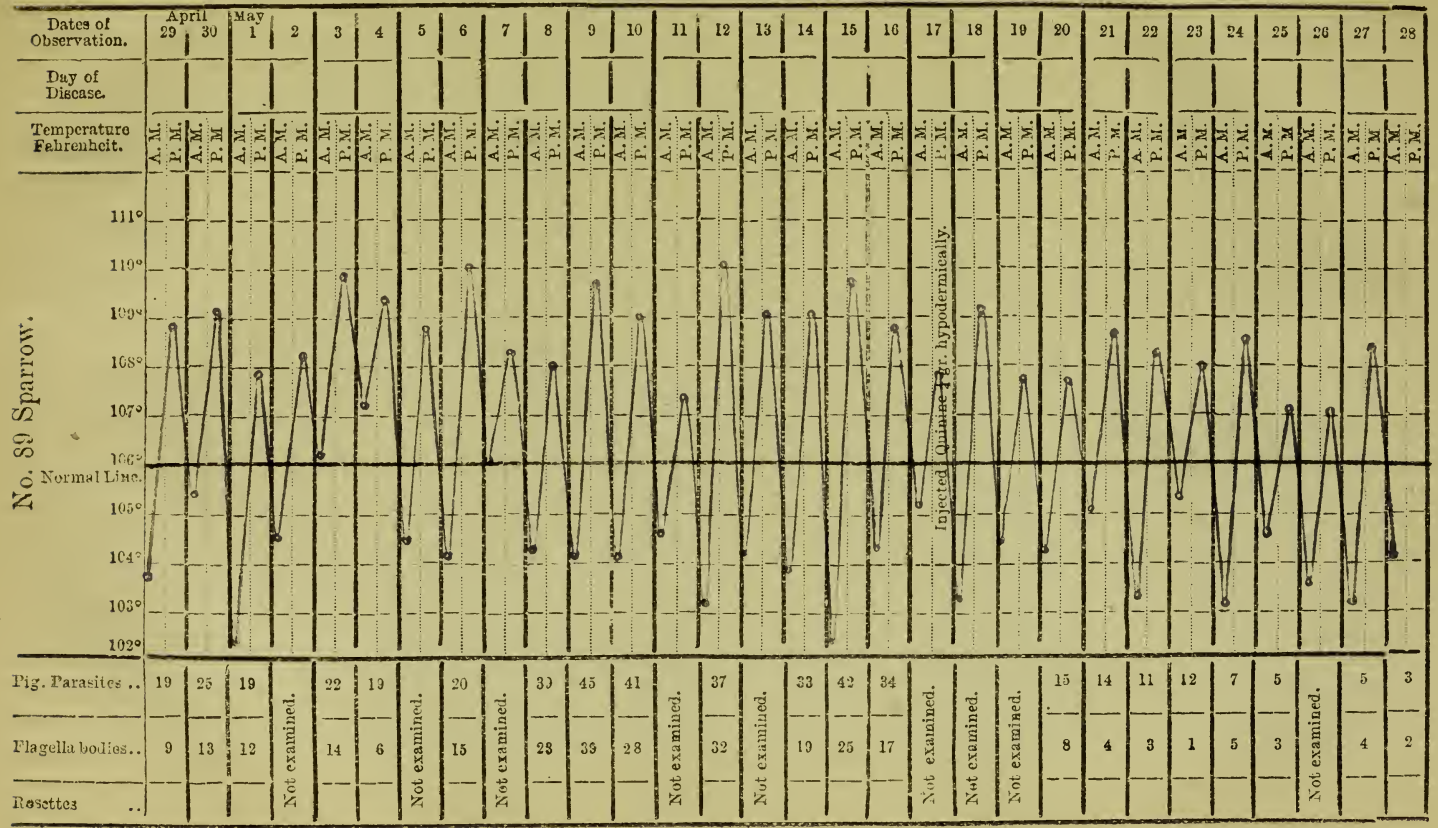
### Normal Temperature of Sparrows.

Charts were kept of a number of sparrows in which no parasites were found and these showed that the temperature was usually about 103 in the morning and 106 in the evening.

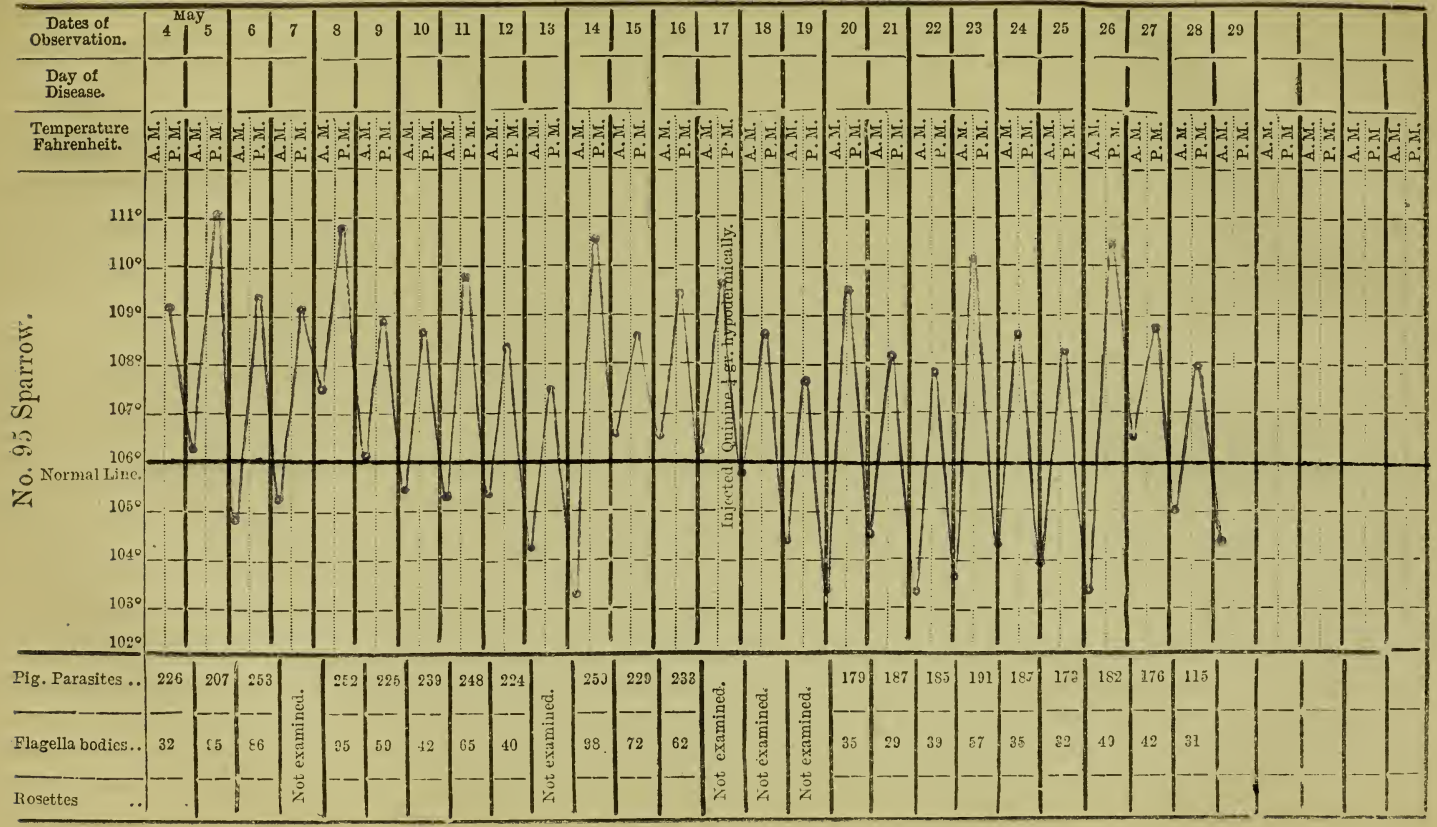
### Quartan Fever in Sparrows.

In the Quartan of man we have often seen that the temperature on the three successive days is "high", "low", "lower", that is, on the first day it is high, next day it is not so high but often a little above normal, and on the third day it is normal; and it is a curious

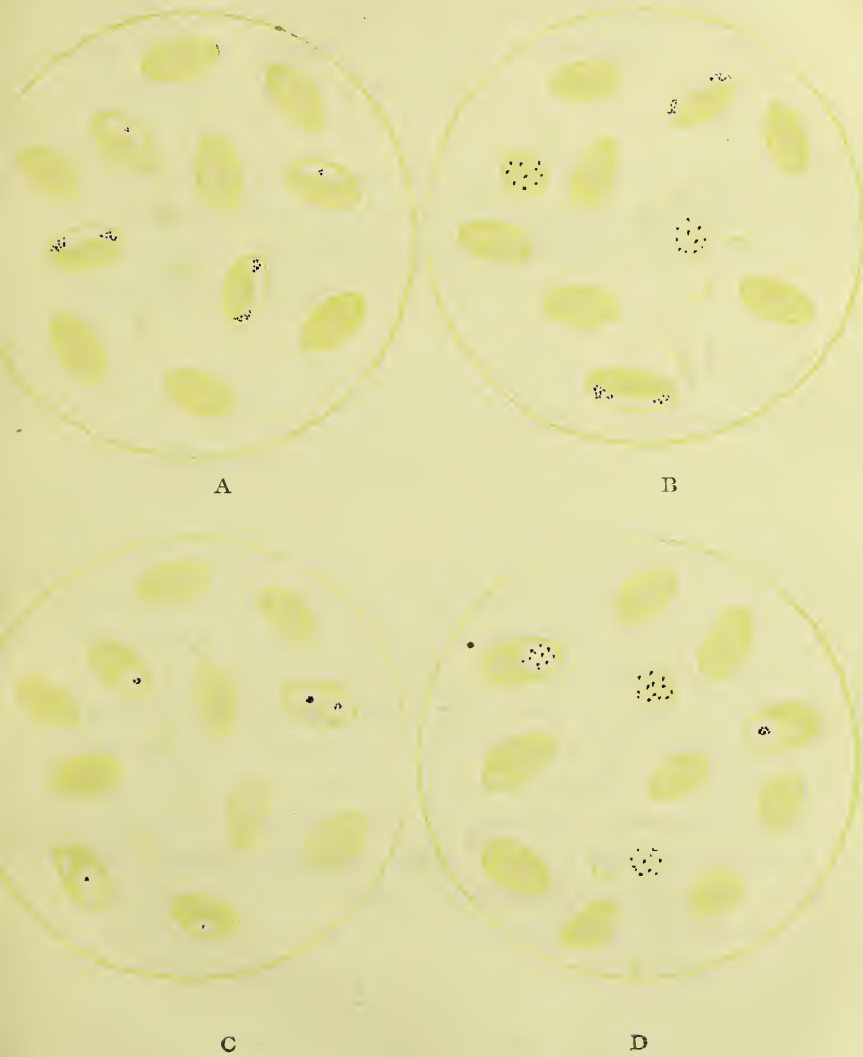
# HALTERIDIUM (QUARTAN) CHART.



# HALTERIDIUM (QUARTAN) CHART.



## SPARROW MALARIA PARASITES.



A B C D

A. Quartan parasites : Halteridium.
B. Ditto Flagella bodies.
C. Tertian parasites : Proteosoma : note how the nucleus is shoved aside.
D. Ditto Flagella bodies and a free flagellum.

thing that in sparrows we nearly always find the temperature on the second day of each period lower than the first day temperature but not so low as the third day temperature. This "high", "low", "lower" temperature applies to each successive cycle of development of the parasites.

The Quartan parasites of the sparrow resemble the Quartan of man in having large granules of pigment and in their slow movement, but they differ in the following points :—

(1) They do not fill the whole red blood corpuscle but lie along one side of the corpuscle, half surrounding the nucleus.

(2) The rosettes are very seldom seen in the sparrow but flagella are seen very often, while in man flagella are rarely seen, but rosettes can always be found in the shivering stage. The exflagellation can be seen in almost every field in some cases. We have frequently put specimens of blood under the microscope as quickly as possible after the blood was drawn in order to see whether it is likely that exflagellation has taken place inside the body. The exflagellated parasite has a fairly definite appearance and we have frequently seen within a minute from the time the blood has been drawn bodies which we believe to be exflagellated parasites, and we are inclined to think that this tends to prove the view which we have advanced in regard to flagella in Malignant Tertian, *viz.*, that exflagellation does take place within the body as well as after the blood has been drawn.

## Sparrow Tertian.

We have before us as we write the charts of 28 sparrows in which Tertian parasites were found and in which the chart shows Tertian fever. The temperatures are frequently about 108° or 109° on one day and 106° or 107° on the next day. In the human Benign Tertian fever we have noticed that there is frequently a change of day in the fever, that is, if the days for fever are the 2nd, 4th, 6th, &c., we may see the fever coming on the 9th, 11th, 13th, &c., and it is a curious fact that a similar change of day is noticed in the case of sparrow Tertian.

## Tertian Parasites.

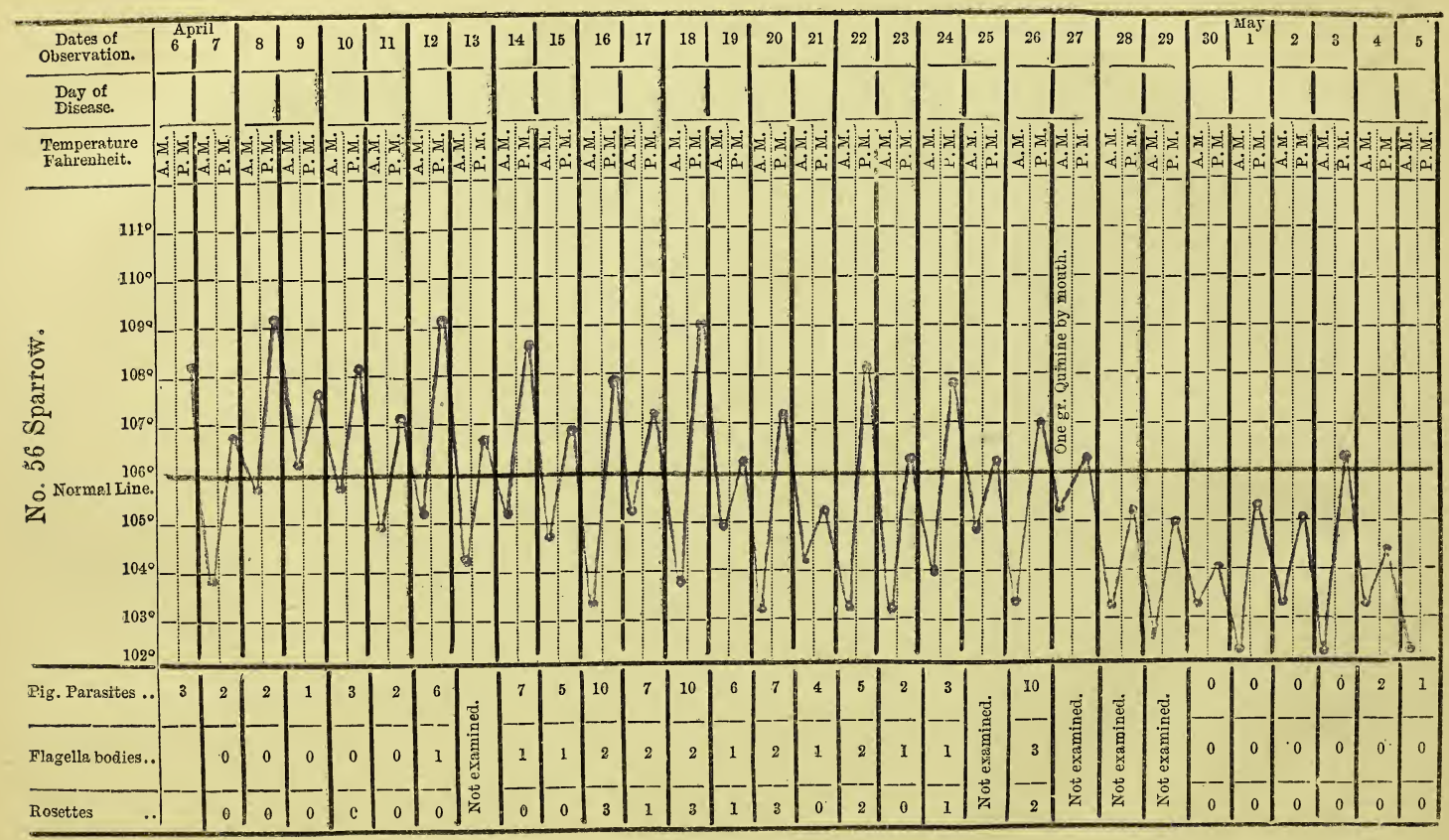
These have been called proteosoma. They are round and rather small, usually placed at one end of the corpuscle and they nearly always push the nucleus of the corpuscle to one side. A Quartan parasite grows along one side of the nucleus but never dislocates it as the Tertian does. In the Tertian the pigment is fine, and the rosette has about 20 parts.

## Effect of Quinine.

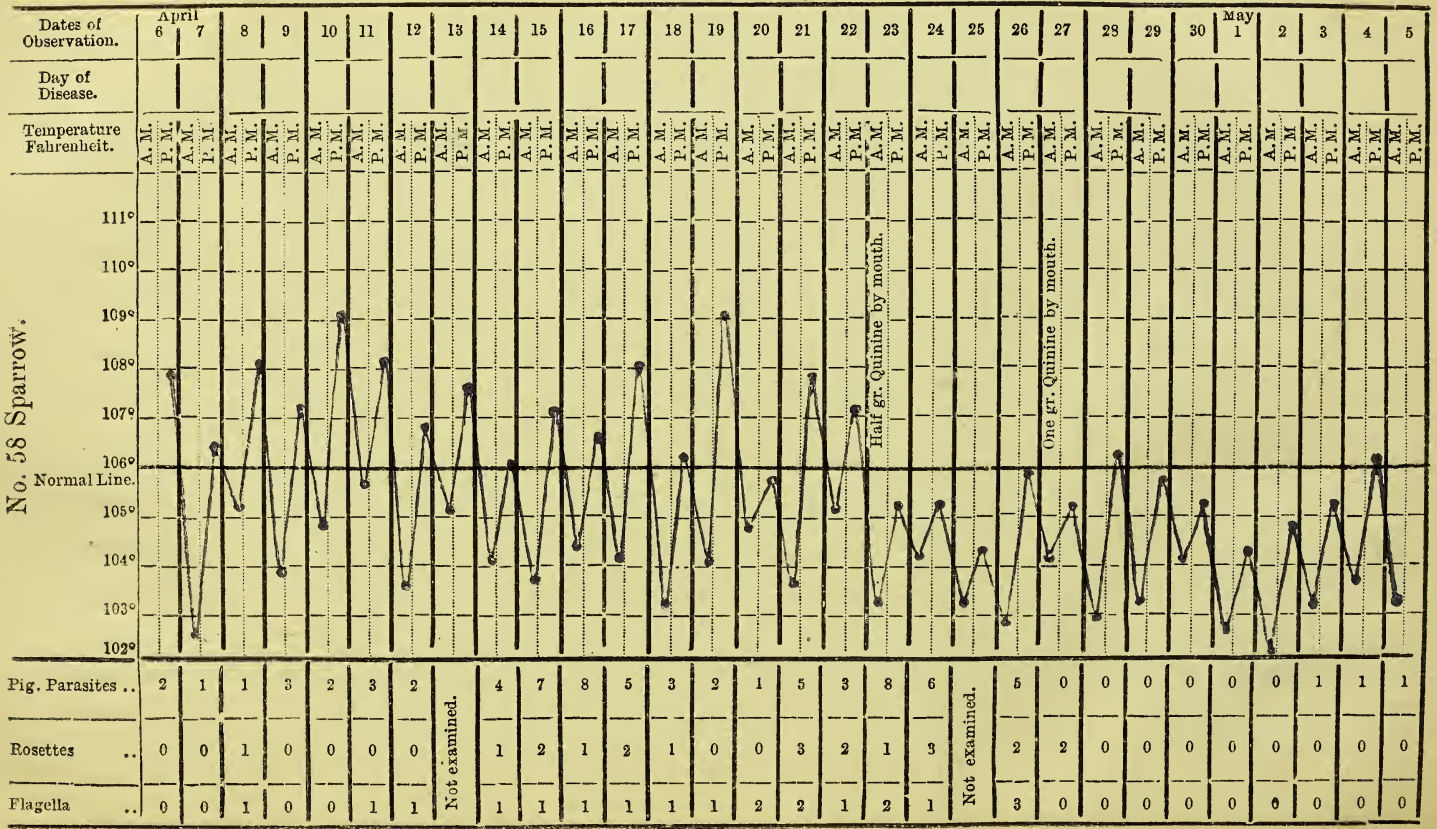
Dr. Lawrie of Hyderabad has said that quinine has no effect on the malarial germs in sparrows. He probably did not experiment on sparrows with Tertian parasites for quinine has a most wonderful effect on these parasites and on the Tertian fever. If we take a few charts we shall see the effect of quinine.

(1) *Sparrow No.* 56.—Here we see between the 6th and 26th April 11 paroxysms in which the temperatures on alternate days went up to 108° or 109°. On the 27th one grain of quinine was given by mouth. From the 28th till the 5th May the temper-

# PROTEOSOMA (TERTIAN) CHART.



# PROTEOSOMA (TERTIAN) CHART.



ature was not above 106°. The number of parasites seen in a five minutes count had been 15: 10: 15: 8: 12: 5: 9: 3: 5: 13: before the quinine was given. The next counts were made on the 3rd, 4th, 5th and 6th days after quinine was given and not a single parasite was seen.

*Case* (2) *Sparrow No. 58.*—In this case there were 9 paroxysms before quinine was given. The paroxysms came on the even days at first—6th, 8th, 10th, and then came on the odd days—11th, 13th, &c. Half a grain of quinine was given by mouth on the 23rd and one grain was given on the 27th. The temperature which had been 107, 108 or 109 on alternate days did not go above 106 for a fortnight. The parasites were not appreciably reduced in numbers after the half grain, but after the grain was given no parasites were seen for 5 days. There had been from 3 to 11 seen daily before the quinine was given. The chart after this again shows a distinctly Tertian type and parasites were again found.

*Case* (3). *Sparrow No. 36.*—After 6 paroxysms in which the temperature on alternate days was 108° half a grain of quinine was given. One paroxysm followed and the number of parasites was not appreciably diminished. One grain was given by mouth and after that no parasites were found and the temperature did not again go above 106°.

*Case (4) Sparrow No.* 67.—Tertian fever up to 108° and 109°. After one grain of quinine the temperature remained below 106° for 6 days. Before giving the quinine, 32 parasites were counted in five minutes.

On the day following the administration of quinine no parasites were found. A few days later the chart shows distinct Tertian and from 13 to 56 parasites were found in the five minutes search.

*Case 15.*—In this case the temperature was 109. One-fifth grain of quinine was given hypodermically Nine parasites had been seen on the day before the quinine was given. Next day 4 were seen, and in the following 9 days only one was seen. Then parasites were again seen and the chart again showed a Tertian appearance. One grain of quinine was then given by mouth. The parasites disappeared and in the next 4 days none were found. The temperature during this time only went above 106 on one day.

The above cases are a few that have been taken at random from a large number, but they are sufficient to show the very marked influence of quinine on the Tertian parasites and fever in sparrows.

We have seen then that at a time of the year when we have been finding Quartan and Benign Tertian parasites in men we have found Quartan and Tertian parasites in sparrows; that the parasites of sparrows in many respects resemble those of man; that the special peculiarity of the Quartan in man, the "high", "low", "lower" temperatureis also well seen in sparrows; that the special peculiarity of the Benign Tertian in man, the tendency to change of day is also well seen in sparrows; that quinine has a marked effect on the Tertian of sparrows; that there are usually about 10 spores in a human Quartan, and there are about 8 in a sparrow Quartan, and that there are about 20 in

a human Tertian, and about the same number in a sparrow Tertian. We have seen here in the Central Provinces very often that the worst cases of fever are found in men who have been working or "shikarring" in the jungles far away from human habitation, and if malarial fever is conveyed from man to man, and from man to man only, how can the excessive severity in such cases be explained?

We do not say that the malaria of sparrows is the same as that of man; but we would ask, is Professor Koch justified in making the pre-supposition that the malaria of man is confined to man and in basing a line of preventive treatment on this assumption before he has proved that the parasites of man are not the same as those of birds or other animals.

## CHAPTER XII.

### THE ANTI-PLASMODISTS.

There are two sides to every question, and while some observers consider that the parasites are the cause of the malarial fevers, there are others who take a contrary view and who do not believe that the small bodies which have been described are parasites at all and that they have nothing to do with the fever. Chief among these is Dr. Lawrie, and it may be worth while to consider the arguments which he has brought forward to prove that these small bodies are not parasites. Dr. Lawrie has written that "the points of controversy between ourselves and the plasmodists cannot be settled by mere assertion and counter-assertion" and we shall enquire whether and to what extent some of the assertions are based on facts.

We have examined about 300 sparrows in the past few months. Two or three men have been employed taking the temperatures under the wing, and four others have been examining the blood of these sparrows daily. The temperatures have been entered in charts and at the foot of the charts the number and kind of parasites seen at each examination have been recorded. There were very few exceptions to the rule that where we found the halteridium we saw a Quartan chart, where we found the proteosoma we found a Tertian chart, and where we found no parasites we found neither a Quartan nor a Tertian chart. The exceptions were a few cases in which the observations were not continued long enough owing to escape or death of sparrows. When then Dr. Lawrie says that the two parasites are the same, is making one of those assertions which he so strongly deprecates.

In the paper which appeared in the *Indian Medical Gazette* in November 1899 Dr. Lawrie said that "the only difference between the proteosoma and the halteridium is that the halteridium is halter-shaped and the proteosoma is round," and in the same paper he says :—"Some remain circular for some time, and somewhat resemble the hyaline bodies seen in human malarial blood. Others soon appear to have a constriction in the centre and contain a few black granules. Most of them become halter-shaped when they attain the full size."

In the sparrows which we have examined, if we found round forms at the beginning in the blood cells we found them throughout the examinations which lasted for some weeks, and if we found the long parasites (halteridium) we also found them throughout. When either parasite is free in the plasma it may be round but while they are within the red blood cells they are perfectly distinct.

Dr. Lawrie then says :—

"Several pigeons were given quinine hypodermically and by the mouth, but without any effect in reducing the numbers of the proteosoma." It is not stated how much quinine was given. We have been told that Quartan fever is not much influenced by quinine and on enquiry have been told that only small doses were given, but we have never seen a Quartan fever which has not been stopped for a time by one dose of twenty grains of quinine. No conclusion of any value can therefore be drawn from the fact that quinine was administered to birds unless the quantity of quinine is known. We have found that one grain of quinine given by mouth to sparrows has a very marked effect in reducing the number of parasites.

We shall next deal with a number of conclusions that have been come to at Hyderabad. It is stated that no form of Laveran body either human or avian is a parasite, and as it fulfils none of Koch's canons, it cannot be "pathogenic."

The first of Koch's canons is "the microbe in question must be found in the blood and tissues of the animal which has suffered from the disease." We have found the Quartan parasite in every case in which we have seen Quartan fever ; we have not seen the Quartan parasite in any case in which the chart did not show Quartan fever ; we have allowed the cases to go for some time for the sake of observing them, and have examined them hundreds and hundreds of times, and we have seen that the parasites are always present while the fever lasts ; when a patient comes into Hospital, if Quartan parasites are seen, this is noted on his ticket, and we have been able in every case to predict from an examination of the parasites that the chart would have a Quartan appearance ; we have been able very often to say on what day the fever would come by the appearance of the parasites ; we have seen in every case that when the shivering begins rosettes will be found in the blood ; and we would ask then is there any other germ which has been credited with the causation of any disease which more thoroughly fulfils Koch's first canon than the parasite which causes Quartan fever ? Further, we have seen how when quinine (twenty grains) is given the parasite of Quartan disappears* and how the fever stops at the same time. And yet we have Dr. Lawrie's assertion that these parasites or Laveran's bodies do not fulfil one of Koch's canons.

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* NOTE.— A few parasites may remain.

There is one of Koch's canons that they do not fulfil, *viz.* that the germ must be translated from culture to culture for several generations, taking precautions against the introduction of other microbes. But here may it not be Koch's canons that are at fault, for although there are many microbes which can be isolated and cultivated for several generations a difficulty arises when we have to deal with the intracellular microbes.

The third of Koch's canons is that the microbe must be capable of causing the disease in a healthy animal. Manson's and Fernside's experiments in transferring Benign Tertian fever from one individual to another are sufficient to convince most people on this point.

Dr. Lawrie next makes the extraordinary assertion that "neither the plasmodium nor the proteosoma possesses the function of reproduction." The men who are working in this Laboratory smiled when they read this "*assertion*" for they have, night after night, put parasites under the microscope, kept them warm near a lamp, watched them develop and form rosettes, and they saw the spores gradually break away.

Dr. Lawrie does not admit however that the young parasites which are seen in the blood cells are the same as the spores which break from the rosettes, and he gives a reason for this assertion, *viz.*, that the "spores are a great deal larger than the speck in the red cell, which is the form in which the proteosoma first appears in the blood." Captain Fernside makes a very reasonable suggestion that measurements might be given to show this alleged difference

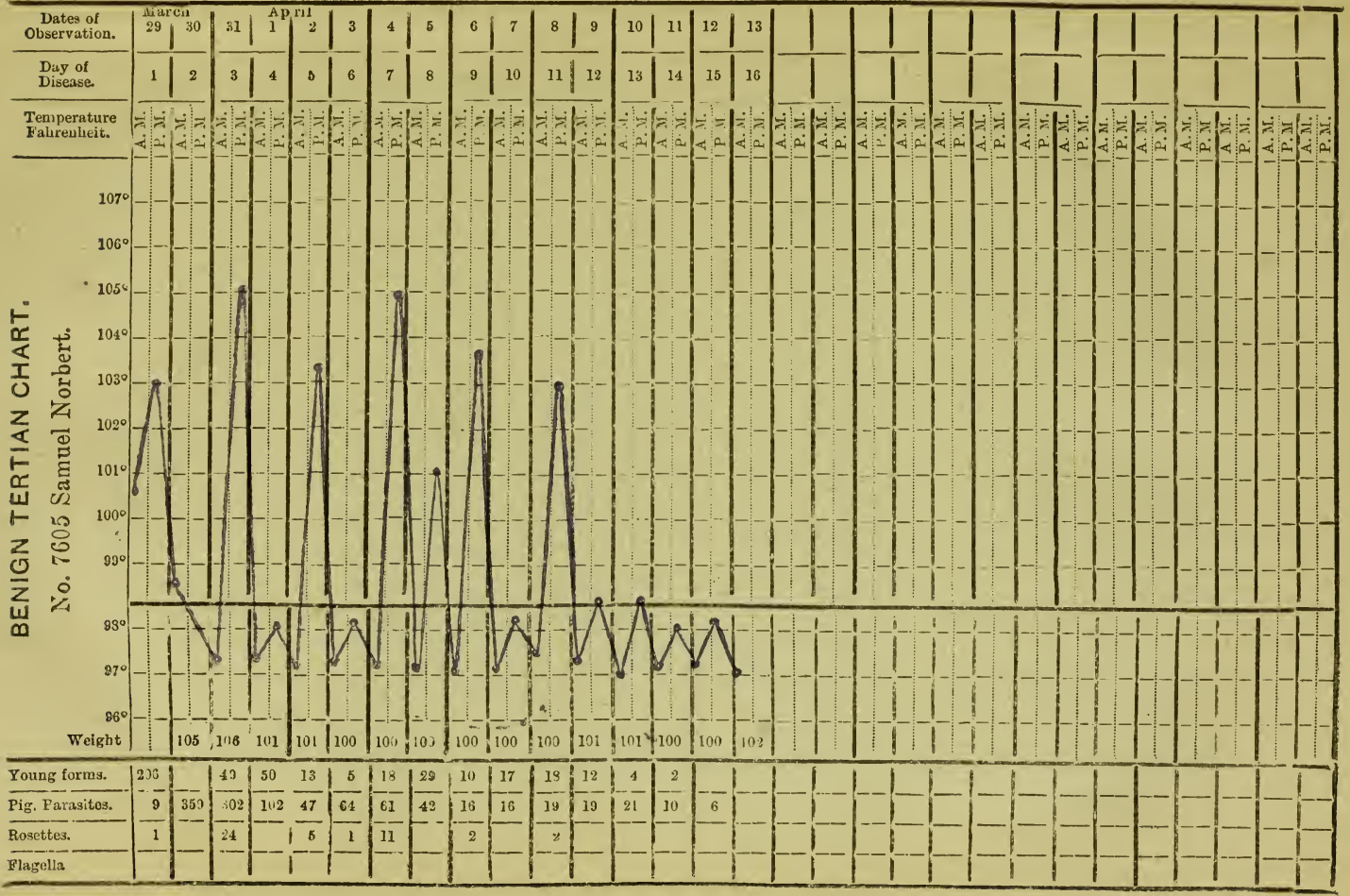
in size. Here, again, Dr. Lawrie calls assertion to his aid and says in reply "the difference in size is so apparent that measurement is unnecessary."

The spores are not all of exactly the same size: some are larger and some are smaller. The spores change apparently in size. We say apparently, for they are subjected to a certain amount of pressure when placed between the cover glass and the slide, and as a result of pressure they may *appear* to increase in size when they have been left between the glasses for some time. Then, again, the young parasite may not be subjected to the same amount of pressure vertically when it is situated inside a corpuscle, and it may be subjected to more pressure laterally and consequently it may appear smaller. For these reasons we think that even if the parasite when it is inside the corpuscle appears smaller than when it is free in the blood plasma, this does not prove that they are different bodies. But this marked difference which Dr. Lawrie appears to have noticed we have not observed.

A Benign Tertian parasite when free in the blood and in the young stage has a peculiar appearance, when it is stained with blue. There is a part which stains well with blue and there is the sac attached to this which stains only at its periphery. Now we get exactly the same appearance in the young parasite after it has entered the corpuscle. It would be interesting to hear how Dr. Lawrie would explain this fact.

The next assertion by Dr. Lawrie is :—

> "We deny altogether that either the halteridium or the proteosoma, or any other form of Laveran body, avian or human, possesses the function of reproduction at all.


BENIGN TERTIAN CHART.
No. 7605 Samuel Norbert.
Dates of Observation.
March
April
29 30 31 1 2 3 4 5 6 7 8 9 10 11 12 13
Day of Disease.
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
Temperature Fahrenheit.
A.M. P.M.
107°
106°
105°
104°
103°
102°
101°
100°
99°
98°
97°
96°
Weight
105 106 101 101 100 100 103 100 100 100 101 101 100 100 103
Young forms.
206 40 50 13 5 18 29 10 17 19 12 4 2
Pig. Parasites.
9 350 302 102 47 64 61 42 16 16 19 19 21 10 6
Rosettes.
1 24 5 1 11 2 2
Flagella

## No. 7605 Samuel Norbert

| Date. | Number of specimen. | Hour when blood drawn. | Temperature. | Young forms unpigmented. | Young forms pigmented. | Middle stage. | Full grown. | Rosettes. | Total. |
|---|---|---|---|---|---|---|---|---|---|
| 29-3-01 | 1 | 11-30 a. m. | 100·6 | 42 | ... | ... | 2 | 1 | 45 |
| | 2 | 1 p. m. | 102·0 | 86 | ... | ... | 2 | ... | 88 |
| | 3 | 3-40 | 102·8 | 37 | ... | ... | 2 | ... | 39 |
| | 4 | 4-5 | 102·8 | 41 | ... | ... | 3 | ... | 44 |
| | | | | **206** | ... | ... | **9** | **1** | **216** |
| 30-3-01 | 1 | 11-15 a. m. | 97·6 | ... | 76 | 2 | 2 | ... | 80 |
| | 2 | 12-15 p. m. | 97·4 | ... | 51 | 29 | ... | ... | 80 |
| | 3 | 2-55 | 97·0 | ... | 37 | 62 | ... | ... | 99 |
| | 4 | 4-20 | 97·6 | ... | 6 | 88 | 6 | ... | 100 |
| | | | | ... | 170 | 181 | **8** | ... | **359** |
| 31-3-01 | 1 | 7-20 a. m. | 97·6 | ... | ... | 12 | 131 | ... | 143 |
| | 2 | 7-50 | 97·8 | 1 | ... | ... | 124 | 1 | 126 |
| | 3 | 9-40 | 103·2 | ... | 1 | 2 | 19 | 23 | 45 |
| | 4 | 11-20 | 103·2 | 48 | ... | ... | 13 | ... | 61 |
| | | | | **49** | **1** | **14** | **287** | **24** | **375** |
| 1-4-01 | 1 | 1 p. m. | 97·0 | 31 | 20 | 2 | ... | ... | 53 |
| | 2 | 1-25 | 97·4 | 17 | 23 | 5 | ... | ... | 45 |
| | 3 | 3-0 | 97· | 2 | 22 | 3 | ... | ... | 27 |
| | 4 | 4-30 | 97·6 | ... | 25 | 2 | ... | ... | 27 |
| | | | | **50** | **90** | **12** | ... | ... | **152** |
| 2-4-01 | 1 | 10 a. m. | 97·2 | ... | ... | 10 | 2 | ... | 12 |
| | 2 | 2 p. m. | 99·0 | ... | ... | ... | 13 | 4 | 17 |
| | 3 | 2-45 | 101 2 | ... | ... | ... | 15 | 1 | 16 |
| | 4 | 4-0 | 103·4 | 13 | ... | ... | 7 | ... | 20 |
| | | | | **13** | ... | **10** | **37** | **5** | **65** |
| 3-4-01 | 1 | 3-30 p. m. | 97· | 3 | 9 | 4 | ... | 1 | 17 |
| | 2 | 4-10 | 98·2 | 2 | 10 | 2 | ... | ... | 14 |
| | 3 | 5-0 | 97·2 | ... | 7 | 11 | ... | ... | 18 |
| | 4 | 8-0 | 97·4 | ... | 5 | 16 | ... | ... | 21 |
| | | | | **5** | **31** | **33** | ... | **1** | **70** |
| 4-4-01 | 1 | 10 a. m. | 98·6 | ... | ... | 2 | 17 | 3 | 22 |
| | 2 | 10-45 | 101·4 | ... | ... | ... | 25 | 7 | 32 |
| | 3 | 12-8 p. m. | 105·4 | 7 | ... | ... | 12 | 1 | 20 |
| | 4 | 2-0 | 103·0 | 11 | ... | ... | 5 | ... | 16 |
| | | | | **18** | ... | **2** | **59** | **11** | **90** |
| 5-4-01 | 1 | 10 a. m. | 97·2 | 4 | 7 | ... | 2 | ... | 13 |
| | 2 | 12-0 | 97·6 | 9 | 10 | ... | 1 | ... | 20 |
| | 3 | 2 p. m. | 98 0 | 6 | 9 | ... | ... | ... | 15 |
| | 4 | 4-0 | 101·2 | 10 | 12 | ... | 1 | ... | 23 |
| | | | | **29** | **38** | ... | **4** | ... | **71** |

Duration of each examination 20 minutes.

(Continud.)

| Date. | Number of specimen. | Hour when blood drawn. | Temperature. | Young forms unpigmented | Young forms pigmented. | Middle stage. | Full grown. | Rosettes. | Total. |
|---|---|---|---|---|---|---|---|---|---|
| 6-4-01 | 1 | 11 a. m. | 97·6 | 1 | ... | ... | 8 | ... | 9 |
| | 2 | 12-0 | 98·0 | 3 | ... | ... | 4 | 2 | 9 |
| | 3 | 2-15 p. m. | 100·6 | 5 | ... | 1 | 1 | ... | 7 |
| | 4 | 2-38 | 101·0 | 1 | ... | .. | 2 | ... | 3 |
| | | | | **10** | ... | **1** | **15** | **2** | **28** |
| 7-4-01 | 1 | 10 a. m. | 97·0 | 3 | 4 | 1 | ... | ... | 8 |
| | 2 | 11 a. m. | 97·4 | 4 | 2 | ... | ... | ... | 6 |
| | 3 | 12-15 p. m. | 97·6 | 6 | 3 | .. | ... | ... | 9 |
| | 4 | 12-40 | 97·8 | 4 | 5 | 1 | ... | ... | 10 |
| | | | | **17** | **14** | **2** | ... | ... | **33** |
| 8-4-01 | 1 | 10 a. m. | 98· | ... | .. | 1 | 8 | 2 | 11 |
| | 2 | 12-0 | 103·0 | 1 | ... | 2 | 3 | ... | 6 |
| | 3 | 12-30 p. m. | 104·0 | 5 | | | 2 | ... | 7 |
| | 4 | 4-0 | 100·6 | 12 | ... | .. | 3 | ... | 15 |
| | | | | **18** | ... | **3** | **16** | **2** | **39** |
| 9-4-01 | 1 | 9 a. m. | 97·2 | 3 | 3 | 2 | ... | ... | 8 |
| | 2 | 1-24 p. m. | 97·6 | 3 | 4 | 2 | ... | ... | 9 |
| | 3 | 3-35 | 98·0 | 2 | 3 | .. | ... | ... | 5 |
| | 4 | 4-0 | 98·0 | 4 | 2 | 3 | ... | ... | 9 |
| | | | | **12** | **12** | **7** | ... | | **31** |
| 10-4-01 | 1 | 8-45 a. m. | 97·2 | ... | .. | 3 | 2 | ... | 5 |
| | 2 | 10-40 | 97·4 | 1 | ... | 2 | 2 | ... | 5 |
| | 3 | 3 p. m. | 97·8 | 3 | ... | 2 | 3 | ... | 8 |
| | 4 | 3-33 | 98·0 | ... | 1 | 2 | 4 | ... | 7 |
| | | | | **4** | 1 | **9** | 11 | ... | **25** |
| 11-4-01 | 1 | 9 a. m. | 97·8 | 1 | 1 | 1 | 1 | ... | 4 |
| | 2 | 10 | 97·6 | ... | ... | 2 | 1 | ... | 3 |
| | 3 | 1-18 p. m. | 97·2 | 1 | 2 | ... | ... | ... | 3 |
| | 4 | 2-0 | 97·4 | ... | ... | 1 | 1 | ... | 2 |
| | | | | **2** | **3** | **4** | **3** | ... | 12 |
| 12-4-01 | 1 | 11-22 a. m. | 97·6 | ... | ... | 2 | ... | ... | 2 |
| | 2 | 1-5 p. m. | 98·0 | ... | 1 | ... | ... | ... | 1 |
| | 3 | 2-48 | 97·4 | ... | ... | 1 | ... | ... | 1 |
| | 4 | 3-40 | 97·8 | ... | 1 | 1 | ... | ... | 2 |
| | | | | ... | **2** | **4** | ... | ... | **6** |
| 13-4-01 | 1 | 9 a. m. | 97·0 | ... | ... | 1 | ... | 1 | 2 |
| | 2 | 9-50 | 97·6 | ... | ... | ... | 1 | ... | 1 |
| | 3 | 12-0 | 97·6 | ... | ... | 1 | ... | ... | 1 |
| | 4 | 2 p. m. | 97·0 | ... | ... | ... | ... | ... | ... |
| | | | | ... | ... | **2** | **1** | **1** | **4** |
| 14-4-01 | 1 | 9 a. m. | 97·6 | 1 | ... | 1 | ... | ... | 2 |
| | 2 | 1 p. m. | 97·8 | ... | ... | 1 | ... | ... | 1 |
| | 3 | 3-0 | 98·0 | ... | ... | ... | ... | ... | ... |
| | 4 | 5-0 | 97·2 | 1 | ... | ... | ... | ... | 1 |
| | | | | **2** | ... | **2** | ... | ... | **4** |

> The rosette is met with so very rarely in the blood, either of birds or of human beings, that it is impossible to regard it as the sporulating element by which reproduction is carried on, and when it is found, the proteosoma forthwith diminish instead of increasing in number."

There are three assertions in this sentence, and following out the principles laid down by Dr. Lawrie we shall avoid counter-assertion; but we would ask attention to one case of Benign Tertian and leave our readers to conclude for themselves what value is to be attached to these three assertions. The chart of the case is given and the record of the blood examinations is also given below. Four slides were examined daily and 20 minutes was devoted to each examination.

At the foot of the chart is shown the number of young forms, pigmented parasites, rosettes and flagella forms which were seen each day; but it is only when we examine the daily record carefully, and note what kind of parasites are seen at a particular stage of the fever, that we are able to see in what way the life history of the parasite is connected with the fever. People who have Tertian fever frequently get fever every day, especially towards the end of the fever, and we often hear them say "but I cannot have Tertian fever, for the fever comes on every day." In this case after 4 turns of fever on the regular days there was some fever on one of the intervening days, and it is worth noticing what parasites were seen on this day, the 5th of April. If, for convenience, we speak of the day on which fever comes as the *fever* day and the intervening day as the *free* day, we see on the 29th, 31st, 2nd

April, 4th (the fever days) that after the paroxysm we find several young unpigmented forms in the corpuscles, and on the *free* days (30th, 1st, and 3rd), we see that the young unpigmented forms get less as the day goes on, and in the evenings there are none; but on the 5th which we should expect to be a *free* day 10 young unpigmented forms were found at 4 P. M. There was a little fever on this day, and some young unpigmented forms were found. It is reasonable to conclude that some rosettes had broken up on this day and that this was the cause of the fever.

On the 30th, a free day, we see a large number of young pigmented forms and a large number of half grown parasites. In the morning the majority are young pigmented and in the evening the majority are half grown. Note the figures at each examination :—

Young pigmented : 76 : 51 : 37 : 6.

Half grown : 2: 29 : 62 : 88.

On the next day, 31st, the young pigmented are scarcely to be seen; there are a few half grown in the morning, and a large number of full grown. At 9-40 the patient began to shiver and 23 rosettes were counted. Several others were seen by Captain Watson who happened to be in the Laboratory at the time, but these are not entered in the record as only those seen at the regular examinations have been noted. At 11-20, 48 young unpigmented forms were seen.

The 1st of April was a *free* day, and we see the young unpigmented forms fairly numerous in the morning but decreasing during the day, several young pigmented forms but no full grown or rosettes. The

2nd was a *fever* day, and we find in the morning the majority of parasites in the middle stage. At 2 P. M. fever came on and we find chiefly full grown and rosettes. In the evening the full grown and rosettes are much less, but we see the young unpigmented forms again taking their place.

On the 3rd, a *free* day, we see the young unpigmented forms getting less and disappearing, the young pigmented forms in the majority and getting less as the day goes on, while the half grown are in small number in the morning but increasing in the evening. There were no full grown, and only one rosette. It is worth noting that this was the first rosette which was found on a *free* day, and it shows that a little irregularity was beginning.

On the 4th, which was a fever day, there were no young forms seen in the morning. Fever came on between 10 and 11 o'clock and rosettes were found together with a number of full grown. In the evening the full grown have decreased, and the young unpigmented have appeared.

On the 5th, which in the ordinary course we should expect to be a free day, we find something unusual; there were 4 full grown forms and there were 10 young unpigmented forms in the evening, showing that there was a certain amount of irregularity of development, and it was on this day that fever came, on what we might expect to be a free day.

The total number of parasites counted on each day was as follows:—

| 29th | 30th | 31st | 1st | 2nd | 3rd | 4th | 5th | 6th | 7th | 8th | 9th | 10th |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 216 | 359 | 375 | 152 | 65 | 70 | 90 | 71 | 28 | 33 | 39 | 31 | 25 |

There was no fever after the 10th and it is worth noting how many parasites were found :—

| 11th | 12th | 13th | 14th |
|---|---|---|---|
| 12 : | 6 : | 4 : | 4 : |

Dr. Lawrie's name ranks among the highest as a Surgeon; but it is hoped that his name as a Surgeon will not put him in the false position of being considered an authority on Malaria.

## CHAPTER XIII.

## QUOTIDIAN.

Manson and Celli both describe two kinds of parasites which cause Quotidian fever, one an unpigmented parasite and the other a pigmented parasite. On the other hand Koch in his Final Report on the German Malarial Expedition says that apart from Quartan and Tertian which occur among ourselves, there is really only one form of malaria, *viz.* "Tropical Malaria." We have not found any parasites that would correspond with Celli's Unpigmented Quotidian, but we have found a few that seem to be the Pigmented Quotidian.

Manson says in regard to Pigmented Quotidian that it is smaller than the Tertian, that it occupies from about one-fifth to one-third of the red blood corpuscle, that the young forms are very active and tend to assume the ring forms, and that the rosette forms little heaps of very minute spores. Celli says the granules of pigment are scarcely visible.

In those we have seen there is little if any appreciable difference in size as compared with the Malignant Tertian, the young forms are more active than the Malignant Tertian, they tend to assume the ring forms, and the number of spores in the rosette are from 6 to 8. We have seen the pigment in fairly distinct rods in one case.

*Crescents.*—In some cases the crescents appeared to be larger and the pigment in more distinct rods than in Malignant Tertian. In one case they were found on the 7th day from the commencement of the

fever and the first day on which the temperature was normal. In one case they were found on the 8th day and one day before the temperature was normal.

*Flagella.*—In one case they were found on the 9th and 11th day and there was slight fever on the 11th, in another on the 14th day, and there was slight fever on the 12th, 13th and 14th.

*Symptoms.*—There appeared to be less sweating and more pain in the joints than in the other fevers, but as the number under observation was very small these symptoms may not be general in Quotidian cases.

# CHAPTER XIV.

## MOSQUITOES AND MALARIA.

The literature on the subject of the relation between Malaria and Mosquitoes is already very extensive, and no attempt will be made here to give a full or connected account of the reasons which led Manson to suggest that Malaria was conveyed by mosquitoes or that led Ross to prove that mosquitoes are the carriers. Our readers may refer for information on this subject to Manson' book on Tropical Diseases, to Ross' West African Report, to Celli's book on Malaria, to Christy's book on Mosquitoes and Malaria, to Giles's book on Mosquitoes and to the numerous articles which have appeared in medical and non-medical Journals during the past year for information on this subject. Some experiments have been made in Nagpur in order to show whether the views which have been advanced by some of the writers mentioned above are correct and a short account of some of these experiments may be of interest.

The mosquito which has got the credit of carrying the Malaria fever germ is called anopheles, and after finding the anopheles we began to enquire what time of the year the anopheles is found and whether the time of its presence tallies with the time when the malarial fevers are prevalent. A year has now elapsed since we began to collect anopheles and a record has been kept of the number caught daily in a given area. The place selected was the Jail Hospital and the following table shows the numbers collected in each month between October 1900 and October 1901.

| Month and year. | Monthly total of admissions for fever. | Monthly total of Anopheles caught. | Lowest record by wet minimum thermometer. |
|---|---|---|---|
| October 1900 ... | 105 | 117 | 56 |
| November ,, ... | 34 | 139 | 51 |
| December ,, ... | 125 | 189 | 52 |
| January 1901 ... | 52 | 43 | 45 |
| February ,, ... | 26 | 18 | 45 |
| March ,, ... | 23 | 16 | 55 |
| April ,, ... | 24 | 15 | 56·4 |
| May ,, ... | 7 | 12 | 60 |
| June ,, ... | 7 | ... | 62 |
| July ,, ... | 12 | 19 | 69·5 |
| August ,, ... | 21 | 1,106 | 70 |
| September ,, ... | 119 | 633 | 64 |

*Weekly totals for August and September.*

| | | |
|---|---|---|
| *August 1901.* | | |
| 1st week ... | 5 | 59 |
| 2nd ,, ... | 3 | 211 |
| 3rd ,, ... | 4 | 382 |
| 4th ,, ... | 9 | 454 |
| Total ... | 21 | 1,106 |
| *September.* | | |
| 1st week ... | 21 | 293 |
| 2nd ,, ... | 38 | 117 |
| 3rd ,, ... | 22 | 114 |
| 4th ,, ... | 38 | 109 |
| Total ... | 119 | 633 |

In the months of February to July there was hardly an anopheles to be found. They began to appear in large numbers about the middle of August, and at the end of August the malarial fevers began to prevail.

The next question is what time are malarial fevers most prevalent, and here it will be interesting to compare the seasonal prevalence of malarial fevers with that of other countries. Celli gives the figures showing the number of admissions for malarial fevers into the hospitals of Rome for thirteen years. If we omit the units and tens, and put down the even hundreds the figures stand as follows :—

| Jan. | Feb. | Mar. | Ap. | May. | June. | July. | Aug. | Sep. | Oct. | Nov. | Dec. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 46: | 37: | 39: | 39: | 35: | 25: | 88: | 176: | 152: | 127: | 95: | 66 |

In Nagpur the average number of admissions for ten years in the Jail with a population of about 1000, is

| Admis- | Jan. | Feb. | Mar. | Apl. | May. | June. | July | Aug. | Sep. | Oct. | Nov. | Dec. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| sions : | 31 : | 27 : | 28 : | 12 : | 15 : | 14 : | 31 : | 38 : | 56 : | 56 : | 50 : | 37 |

In Rome the maximum is generally attained in August. In Nagpur it is later—in September or October. In Rome from November till June there is a general tendency to a diminution of the number of admissions, and the similarity in the Nagpur figures is remarkable.

There has been a great deal of evidence already brought forward to show that in whatever parts of the world malarial fevers are found the anopheles mosquitoes are found there also ; but there probably has not been any experiment made similar to this one, to

show whether the anopheles season coincides with or precedes the fever season.* For some months—April, May, June and July—there were very few admissions for fevers and in those months there was scarcely an anopheles to be found. The anopheles appeared in August and a fortnight or three weeks later malarial cases began to come to Hospital. Then it may be worth while to consider why the anopheles mosquitoes begin to breed in August, and possibly the rainfall may be one of the most important elements to be taken into consideration. The average monthly rainfall omitting decimals at Nagpur for the past 10 years is :—

| | Jan. | Feb. | Mar. | Apl. | May. | June. | July. | Aug. | Sep. | Oct. | Nov. | Dec. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Rainfall : | 0 : | 0 : | 0 : | 0 : | 0 : | 7 : | 14 : | 12 : | 9 : | 1 : | 0 : | 0 |

At page 5 of the West African Report it is shown that the largest number of admissions for malarial fevers occur in the middle of the rainy season. Here the admission rate is greatest after the rains.

We have seen that the seasonal prevalence of anopheles would tend to support the mosquito-malarial theory. Many experiments were made on individuals who volunteered to allow themselves to be bitten and a short account of these will be given.

First it was necessary to get a supply of young anopheles. Every little pool of dirty water around the Jail had numbers of the culex mosquitoes, but the anopheles pools were very few. It has been pointed out by many writers that the anopheles prefers a pool

* Since writing the above a similar record has appeared in October number of the *Indian Medical Gazette* by Captain Glen Liston.

with clean water, while the culex will choose a pool with dirty water, and our observations here confirmed this fact. A cook-house pool is the favourite place for the culex and from one small *tanka* (a small masonry tank) we collected about $4\frac{1}{2}$ millions of culex eggs in a month. The eggs are laid in "boats," each boat being made up of about 250 eggs. Sometimes as many as 1,600 of these boats were deposited on this little *tanka* in a single night, or rather in the early morning which is the laying time. At one corner of the Jail there was a small clear stream coming from an underground drain (a French drain) and this was the favourite place for the anopheles to deposit their eggs. When the stream ceased to flow, a few pails of clear water were thrown into this drain every morning and the anopheles continued to lay their eggs there with great regularity as long as any anopheles were to be found. It need hardly be said that the larvæ from this pool were all collected.

The time taken for development was as follows:— After 48 hours the young larvæ came out of the shell; 16 days later the larvæ were transformed into the nymphæ; and in from two to three days the fully formed mosquito emerged from its covering.

The mosquitoes were kept in large bottles from which the upper part had been removed and these bottles were covered by a cap of mosquito netting. At first the netting used had a coarse mesh, but the anopheles was able to pass easily through this, and then fine mesh netting was substituted.

The males were fed on plantains and the females were allowed to have a meal of blood—(only the

females suck blood)—from the arm of an individual who had a known kind of malarial parasites in his blood.

The time chosen for giving this meal of blood was the evening just after sundown, for then the mosquitoes fed greedily when a man placed his forearm, previously moistened with water, over the top of one of the bottles containing the mosquitoes. The mosquitoes were allowed to bite the same man for 4 or 5 nights and then they were allowed to bite one of those who volunteered to be bitten.

### Experiments with Benign Tertian.

In describing the results it will be well to take each kind of fever separately, and we shall begin with the Benign Tertian. The dates on which the mosquitoes were fed on the individual already infected and the volunteers are here given.

We see that out of seven cases who volunteered to be bitten by the mosquitoes four were attacked by fever, but in only two of these did we find the Benign Tertian parasite. In case (1) a parasite was found but it was a young form and there was no proof that it was a Benign Tertian.

Taking the two cases in which parasites that were undoubtedly those of Benign Tertian were found, we see that the fever came on in one case 22 days after the first bite, and in the other about 15 days after the first bite. It may be said by those who are opposed to the mosquito theory that the fact that the attacks of fever came after the mosquito bites was entirely accidental. This was the objection raised against the cases which were experimented on in Italy. We have

## BENIGN TERTIAN.

| Serial No. | † *B* Name. | **A* Case on which mosquitoes were fed. | Date when fed on *A*. * | No of bites on *A*. | Date when fed on *B*. † | No. of bites. | Date when *B* was attacked by fever. | Kind of parasites found. | Nature of fever. |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Tilak Ram | Narayen ... | 15, 18, 21, 25, 28, 30 December. | 83 | 20, 27, 29, December, 1st January. | 108 | 22, 24, 26, December. | Young form changing shape rapidly. | Distinct Tertian, 3 paroxysms, temperature ranging to about 103 each time; on 28th tem. 103·6. |
| 2 | Ganshia... | Shaikmahboob | 24th to 27th December. | 34 | From 27-12-00 till 8-1-01 every night. | 78 | 10th or 12th (Temp. was not taken till 27th January.) | Pure Benign Tertian. | He had had fever before, but temperature had not been taken as he had not reported sick. |
| 3 | Pahlad ... | Thibroo ... | 3-1-00. | 12 | 9-1-01 till 17-1-01 every night | 22 | 31 1 01 | Typical Benign Tertian. | On 31st January and 1st February temperature went over 101. |
| ,, | ,, | Yeshwanta.. | 26-1-00. | 5 | 30-1-01 to 31-1-01 | | | | |
| 4 | Phundia... | Thibroo ... | 3-1-01 to 7-1-01 | 14 | 9-1-01 to 20-10-01 daily. | 20 | 20 1 01 | *Nil.* | A very large number of eosinophile cells, 6 in a field, and in one field (stained specimen) 32. |
| 5 | Bisnoo ... | Thibroo ... | 1-1-01 to 4-1-01. | 14 | 9-1-01 to 23-1-01. | 44 | *Nil.* | *Nil.* | *Nil* |
| 6 | Motiram.. | Thibroo ... | 27-12-00 to 30-12-00. | 17 | 31-12-00 to 7-1-01. | 16 | *Nil.* | *Nil.* | *Nil* |
| 7 | Changia... | Sadoo ... | 3-1-01 to 6-1-01. | 22 | 9-1-01 to 19-1-01 | 50 | *Nil.* | *Nil.* | *Nil* |

* *A*=the man on whom mosquitoes were fed primarily.
† *B*=the man who was bitten by the infected mosquitoes.

## QUARTAN.

| Serial No. | † *B.* Name. | * *A.* Name. | Date when fed on * *A.* | Number of bites on * *A.* | Date when fed on † *B.* | Number of bites on † *B.* | Date when † *B.* was attacked by fever. | Kind of parasites found. | Nature of fever |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 6610 Sectia | 483 Sitaram | 16th to 19th December. | 15 | 21st to 29th Decr. | 25 | | | |
| | | | 18th to 22nd do. | 16 | 23rd to 31st do | 35 | *Nil.* | *Nil.* | *Nil.* |
| | | | 2nd to 5th Jan. | 31 | 6th to 8th Jan. | 23 | | | |
| 2 | 7413 Ghidoo | Do. | 2nd to 5th do. | 17 | 9th to 21st Jan. | 58 | 5-2-01 | Not distinct. | 102 Temp. |
| | | | 5th to 8th do. | 17 | 9th to 21st do. | 30 | | | |
| 3 | 6474 Nago | Jan Mohomed. | 21st to 25th Decr. | 16 | 25th to 31st Decr. | 38 | *Nil.* | *Nil.* | *Nil.* |
| | | | 29th to 31st do. | 20 | 5th to 9th Jan. | 25 | | | |
| 4 | 7133 Pustan | 2267 Sambhoo | 9th to 13th Jan | 15 | 13th to 17th Jan. | 17 | ,, | ,, | ,, |
| | | | 12th to 15th do. | 38 | 16th to 20th do. | 15 | | | |
| 5 | 7422 Balia | 350 Jangli | 4th to 6th Feb. | 19 | 8th to 17th Feb. | 24 | ,, | ,, | ,, |
| | | | 5th to 7th do. | 16 | 11th to 16th do. | 10 | | | |
| 6 | 7004 Sadaram | Do. | 6th to 8th Feb. | 21 | 9th to 16th Feb | 23 | ,, | ,, | ,, |
| | | | 7th to 9th do. | 7 | 10th to 12th do. | 7 | | | |
| 7 | 7323 Jairam | 382 Panchoo | 4th to 6th Feb. | 11 | 8th to 11th Feb. | 12 | ,, | ,, | ,, |
| | | | 7th to 9th do. | 16 | 10th to 13th do | 5 | | | |
| 8 | 7277 Barkia | Do. | 6th to 8th do. | 31 | 9th to 16th do. | 51 | ,, | ,, | ,, |
| 9 | 3156 Abdul Aziz | 492 Jeolagya | 12th to 16th March. | 24 | 20th to 24th March. | 21 | ,, | ,, | ,, |

* *A*—the man on whom mosquitoes were fed primarily.
† *B*—the man who was bitten by the infected mosquitoes.

carefully examined the blood in every case that has been admitted for fever while these experiments were being carried on, and out of a population of 1,200 (odd) there were only two other cases admitted for Benign Tertian. If the fever in these two cases were not the result of the mosquito bite, would it not be curious that out of seven individuals who were bitten by mosquitoes two should get Benign Tertian fever, while only two other cases occurred among about 1,200 men? and would it not be still more curious that the time when the fever came on was about a fortnight or three weeks after they had been bitten by the mosquitoes?

The fever in all these cases was milder than in the cases which were admitted to hospital without having been bitten voluntarily by mosquitoes. Perhaps the mosquitoes had not been fed originally at a time when the flagella bodies were ripe for giving out flagella, or perhaps there may be other ways in which the malarial parasite can be introduced into the human body.

### Experiments with Quartan.

In the accompanying table are given the details regarding this experiment. Nine men volunteered to be bitten. There were several cases of Quartan fever in the hospital at the time the experiments were made, so the mosquitoes had a good chance of getting the infection into their own bodies. The mosquitoes were allowed to feed on a Quartan case for about four successive nights and they were then allowed to bite the volunteers. Out of the nine cases there was not one that got Quartan fever, and not one in whose blood

Quartan parasites could be found. The blood of all these cases was examined almost daily and if Quartan parasites were present they could hardly have escaped notice. The number of bites varied from 21 to 83, and if Quartan fever is conveyed by anopheles then it would be difficult to understand why these volunteers did not get Quartan fever.

It was in the early months of the year that Quartan cases were found chiefly, although there were a few men in whose blood Quartan parasites could be found at any time of the year, so the season for Quartan infection does not appear to be the same as the season for the Malignant Tertian infection, the Quotidian infection, and perhaps the Benign Tertian infection.

The question will be asked, with what kind of anopheles were these experiments made ? The following different species are found here—Costalis, Funestus, Superpictus, Rossii, but when making the experiments it was not noted what particular species was used.

### Experiments with Malignant Tertian and Quotidian Cases.

Seven men were bitten by anopheles that had been fed on cases that were infected with Malignant parasites. Of these, one got fever (102·8) three days after being bitten and Malignant Tertian parasites were found. In another case no fever was noticed, but 23 days afterwards a crescent was found. In 5 cases no fever followed and no parasites were found in the blood.

Only one experiment was made with Quotidian. The mosquitoes bit a man who was infected with

## MALIGNANT TERTIAN.

| Serial No. | †B Name. | *A Name | Date when fed on *A | Number of bites on *A. | Date when fed on †B | Number of bites on †B | Date when B was attacked by fever. | Kind of parasites found. | Nature of fever. |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 520 Bhagthram. | 274 Sagun. | 15-2-01 | 49 | 19-2-01 | 31 | Nil | Nil | Nil |
| 2 | 529 Indru .. | 7656 Gosai. | 15-2-01 | 43 | 19-2-01 | 48 | ,, | ,, | ,, |
| 3 | 663 Hania .. | 42 Lachmaya. | 16-2-01 | 46 | 19-2-01 | 22 | ,, | ,, | ,, |
| 4 | 7338 Raghoba.. | 83 Narhari. | 17-2-01 | 20 | 21-2-01 | 17 | ,, | ,, | ,, |
| 5 | 7320 Mohan .. | Do. | 17-2-01 | 18 | 21-2-01 | 11 | 24-3-01 | Ring forms (M. T.) | 102·8 Temp. |
| 6 | 7394 Goma .. | 475 Seetia | 18-2-01 | 32 | 21-2-01 | 25 | 16-3-01 | Crescent form | Nil |
| 7 | Bisan .. | Do. | 23-2-01 | 24 | 27-2-01 | 13 | Nil | Nil | Nil |

## QUOTIDIAN

| Serial No. | †B Name | *A Name. | Date when fed on A | Number of bites on *A | Date when fed on †B | Number of bites on B | Date when B was attacked by fever. | Kind of parasites found. | Nature of fever. |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 440 Khunan .. | 5703 Hiralal .. | 9th to 11th Feb. | 45 | 13th to 17th Feb. | 25 | Nil | Nil | Nil |

* A=The man on whom mosquitoes were fed primarily.
† B=The man who was bitten by the infected mosquitoes.

Quotidian parasites, 45 times, and they were allowed to bite a volunteer 25 times. No fever followed and no parasites were found.

What conclusion can be drawn from these experiments ? The evidence in favor of Benign Tertian being conveyed by mosquitoes has been discussed, but as regards Quartan there is no evidence at all that it is conveyed by anopheles. Take, for instance, the case of Seetia, the first on the list. He was bitten 83 times by mosquitoes that had already bitten a man with Quartan parasites, 62 times, and yet no fever followed. If anopheles carry Quartan then it would be difficult to explain why he was not attacked unless we assume that (1) he was immune, or (2) that the anopheles did not bite him at the time when the parasite was in a suitable condition, or (3) that the season was not one in which the Quartan parasite could develop properly, or (4) that the species of anopheles used in the experiment was not the correct one.

Similarly, if we take the first case in the Malignant Tertian list we see that the anopheles bit a man who was infected with Malignant Tertian parasites, 49 times, and 4 days afterwards these same mosquitoes bit a healthy man 31 times and yet no fever followed and no parasites were found in the blood.

On the other hand we have seen that the season when the anopheles are most abundant is just a few weeks before the season when the malarial fevers begin to prevail.

Manson has proved conclusively that the Benign Tertian can be conveyed by the anopheles mosquito, but in regard to the other fevers there is not apparently any evidence that they are carried by mosquitoes, and the only conclusion that may be fairly drawn from the experiments that have been made here is that a man may be bitten very often by mosquitoes which have been already fed on an individual who has undoubtedly Quartan or Malignant Tertian parasites in his blood and yet not suffer from an attack of fever nor have any parasites in his blood.

The whole subject is one which requires to be much more fully investigated.

## CHAPTER XV.

## SEASONAL PREVALENCE OF MALARIAL FEVERS.

We have already seen that the time of the year when the malarial fevers are most prevalent is in the months of September and October and that the number then gradually diminishes. In Italy the fevers have been divided into two groups, one called the Æstivo-autumnal and the other the Spring fevers. In the former the Italians put the Malignant Tertian and Quotidian and in the latter the Quartan and Benign Tertian. We propose here to enquire what kinds of malarial fever prevail at particular seasons, and in the table given below the total number of admissions for each kind of fever during the past ten months have been entered.

*Statement showing number of admissions by months with different varieties of parasites.*

| Month. | Quartan. | B. Tertian. | M. Tertian. | Quotidian. | Double infection. | | Total. |
|---|---|---|---|---|---|---|---|
| | | | | | M. T. and B. T. | M. T. and Quot. | |
| November 1900. | ... | ... | ... | ... | ... | ... | ... |
| December ... | 3 | 5 | 24 | ... | ... | ... | 32 |
| January 1901 ... | 4 | 3 | 16 | 1 | ... | 1 | 25 |
| February ... | 1 | ... | 12 | ... | ... | 1 | 14 |
| March ... | 1 | ... | 5 | ... | ... | ... | 6 |
| April ... | 1 | ... | ... | ... | ... | ... | 1 |
| May ... | ... | ... | ... | ... | ... | ... | 0 |
| June ... | ... | 3 | ... | ... | ... | ... | 3 |
| July ... | ... | 3 | ... | ... | ... | ... | 3 |
| August ... | 1 | 3 | 10 | ... | ... | ... | 14 |
| September ... | 1 | 39 | 51 | 2 | 3 | ... | 96 |
| October ... | ... | ... | ... | ... | ... | ... | ... |
| Total ... | 12 | 56 | 118 | 3 | 3 | 2 | 194 |

## Quartan.

There were altogether 12 Quartan cases excluding those with mixed infections. From May to July no Quartan case was admitted. Some of the men who had been admitted during the cold weather had Quartan parasites in their blood throughout the greater part of the year although they were not getting Quartan fever. One of those who was admitted in September and had Quartan parasites in his blood was an old case (Jangli) who had been in hospital in the winter time; he got an attack of Influenza in September, so his admission might have been shown under Influenza rather than under Quartan.

## Benign Tertian.

In the first eleven days of September there were 18 admissions for Benign Tertian whereas there were only 11 admissions for Malignant Tertian in the same time. Between the 11th and the end of September the number of admissions for Benign Tertian was only 21 while the number admitted for Malignant Tertian was 40; but during this latter period a weekly dose of quinine, xx grains, was given to 400 men, and it will be shown later on that this weekly dose of quinine had probably a greater effect in checking the Benign Tertians than the Malignant Tertians. As there were however in the month of September nearly as many Benign Tertians as there were of Malignant Tertians, the numbers being 39 Benign to 51 Malignant, it would seem that the term æstivo-autumnal which the Italians have applied to the Malignant Tertian is misleading. In January, February and March there were many more Malignant Tertians than Benign

Tertians so the term Spring Tertian applied by the Italians to the Benign Tertian is also not a good term. Various names have been given with a view to distinguishing the parasites. If you say to a man with a temperature of 107 that he is suffering from *Benign* Tertian he will probably be very indignant and consider that you are making jokes on a subject which he is not inclined to laugh at. Some have applied the terms Tertian and Semi-Tertian, but taking everything into consideration we think that the most suitable names would be Crescent Tertian and non-Crescent Tertian.

### Malignant Tertian.

From April to July there were no admissions for Crescent Tertian. They began to appear in August and were most numerous at the end of September.

### Quotidian.

The number of these was very small—about three altogether, of which two occurred in September.

## CHAPTER XVI

### TREATMENT AND PROPHYLAXIS.

A man may have a large number of parasites in his blood and yet have no fever while they are growing. It is only when the rosettes burst, and the spores break away, or when the flagella bodies break up, that fever comes on. Hence it is supposed, that the fever is due to some poison which has been excreted by the parasite during its growth and that this poison does not affect the individual injuriously until it has been liberated by the breaking up of the rosette. This has not been proved by experiment, but it seems to be a reasonable explanation of what occurs. Treatment then resolves itself into two parts—first the removal of the poisonous material excreted by the parasites, and second the destruction of the parasites.

The removal of the poisonous material is effected naturally by the free sweating which follows an attack, and it is assisted by the various diaphoretics or purgatives which are administered in such cases, or by hot drinks. This part of the subject is dealt with fully in the ordinary Medical text books and no advantage would be gained by its repetition here.

The parasites are not got rid of through the sweat glands and we have to consider how they can be killed or cleared out. Nature has supplied a remedy in the shape of the phagocytes and they are constantly destroying some of the parasites. The medicines that are used to assist in their destruction are quinine, arsenic, and methylene blue. We have

shown in the Chapter on Quartan fevers the absolute inefficiency of arsenic, and although we have not carried out a similar series of experiments to show whether arsenic has any effect in killing the other parasites still we are not aware of any experiment that has been made to prove that arsenic is of the slightest use. Arsenic acts as a tonic, and in that way it may ultimately be useful as a paraciticide, but there does not appear to be any proof that it is effectual. The two remedies that are relied on now are quinine and methylene blue.

No one doubts the efficacy of quinine, and it may be asked, why should we bother about another remedy as long as we know that quinine is effectual. There are three reasons:—methylene blue is cheaper, it can be produced artificially in large quantities, and there are some conditions in which a patient cannot bear quinine. One of these is pregnancy. A dose of three grains of quinine and followed by three in the evening has been found to cause very troublesome contractions of the uterus, and it was only by the administration of the tincture of opium that such contractions were stopped. In such cases it is with the greatest hesitation that one can venture to give even small doses of quinine, and we should be glad to find another drug that would act as well in causing the death of the parasites, while it would not set up contractions of the uterus.

## Quinine.

We have already seen that there is no disease in which the effect of a drug can be so thoroughly tested as in Quartan fever. Its great regularity and its

liability to recurrence make it an exceptionally simple disease for experimental purposes. Twenty grains of quinine given on the first day, the second day, or on the third day of the cycle of development will stop the paroxysms for a time. But although it is easily stopped there is probably no parasite so persistent inasmuch as a few parasites may be found for months after the original attack of fever. We have been able to find the Quartan parasites, but in very small numbers in cases that were under observation for Quartan over six months ago. These cases had received only one dose of quinine and they were kept under observation from time to time for several months. In order to completely extirpate the Quartan parasites it would be necessary to give repeated doses of quinine at intervals of a week or so.

Most cases of Benign Tertian can be stopped in a day by quinine, but the doses required are probably a little larger than for Quartan. However, a good deal depends on the number of parasites found. The Malignant Tertian is the most difficult to deal with. If it is a mild case with only a few parasites it may be stopped quickly with quinine; but a severe case with a large number of parasites will not be readily checked. The important point in the treatment is to give doses sufficiently large to prevent the formation of crescents and to prevent the secondary or flagellar fever. It will often be necessary to give as many as forty grains in the day to an adult for this purpose.

We have given forty grains in one day to a Malignant Tertian case, and yet the fever was not stopped, and the Flagellar fever came on. The

quinine was not however given at the commencement of the fever. In others a dose of twenty grains a day for several days has not been sufficient to check the formation of crescents. In one case the formation of crescents was checked by giving forty grains on the first day, thirty on the second, twenty on the third, and then ten grains daily for some days. But the dose should be regulated by the severity of the case and the number of parasites found. Captain Johnston, I. M. S., has found that the formation of crescents can be prevented by the hypodermic injection of quinine, but if the crescent formation can be checked by the administration of quinine by mouth, few people will be willing to submit to the hypodermic method even though a smaller dose is required.

The enormous benefit to be derived from the use of quinine can scarcely be exaggerated. There is probably no medicine employed to check any disease that can compare with it, and although one has always had a certain amount of belief in its value, it is only after a long series of experiments that we begin to realize its wonderful power. There is no medicine so useful when properly used, but there is probably no medicine which is so much abused. How often do we see it given at random in cases which are not malarial at all, and in which it may probably do much harm, for although not a poison in ordinary doses, still its effects are to a certain extent poisonous, and it is only when we are certain that there are malarial parasites present that its use in very large doses is at all justifiable.

Many experiments have been made with methylene blue in Quartans and the two Tertians. When it is given the patient should always be warned that it will

turn the urine blue. It is excreted by the kidneys, and it is liable to cause some irritation and pain in the kidneys. It has been given in doses of 3 grains three times a day. Quartans and Benign Tertians are stopped by it, but not so certainly nor so quickly as by quinine. Its effect in Malignant Tertians is being tried at present.

## Prophylaxis by Mosquito Nets.

In the March number of the *Practitioner* Manson gives an account of the experiments which have been made in Italy by inducing men to live in mosquito-proof houses and the results of the experiments are very strongly in favor of the Mosquito Malarial theory. In most of the cases there was a check experiment, that is, there were some people at the same places who did not live in mosquito-proof houses. If we put down a few of the figures showing on the one side the number protected by mosquito curtain and the number of cases of fever that occurred among them, and on the other side the number unprotected and the number of cases of fever that occurred among them, the difference in the incidence of fever is very striking, thus :—

| *Protected.* | | | *Unprotected.* | |
|---|---|---|---|---|
| Number. | | Got fever. | Number. | Got fever. |
| 52 | ... | 2 | | Almost every one. |
| 52 | ... | 0 | 51 | Only 7 escaped. |
| 36 | ... | 2 | 52 | Only 7 escaped. |
| 30 | ... | 2 | 37 | Only 2 escaped. |
| 104 | ... | 3 | 25 | All got fever. |

These are only a few of the results of the experiments which Manson gives, but they serve to show the

enormous value of the mosquito curtain. The mosquito curtain may act by keeping out mosquitoes, or it possibly may act by keeping out some germs that are borne by the air. The fact that Benign Tertian has been proved to be conveyed by mosquitoes would favor the former view; whereas the fact that in our experiments so many men have been bitten by infected mosquitoes and yet such a small proportion of them got fever might be held to favor the latter view.

### Prophylaxis by Quinine.

We have frequently given small doses of quinine to one lot of men during the fever season while another lot received no quinine, and we have compared the number of admissions from each lot. A similar experiment is being made in the present year but with this difference, that the kind of parasite found in those who are admitted from each group is recorded, and instead of giving small doses three or four times a week one dose of twenty grains is given once a week. The experiment was begun on the 11th September. The twenty-grain dose was given to 400 men once a week and the weekly totals of admissions from these 400 are given in the table below. The total number of admissions from the remainder, about 600 to 700, are also given :—

| | *Received quinine.* | | | | *Not receiving quinine.* | | | |
|---|---|---|---|---|---|---|---|---|
| | Quart. | B. T. | M. T. & Quot. | No parasite. | Quart. | B. T. | M. T. & Quot. | No parasite. |
| 1st week ... | 0 | 3 | 7 | 1 | 0 | 7 | 8 | 11 |
| 2nd week ... | 0 | 0 | 2 | 1 | 0 | 2 | 16 | 8 |
| 3rd week ... | 1 | 0 | 1 | 4 | 1 | 9 | 8 | 30 |
| 4th week ... | 0 | 0 | 4 | 6 | 1 | 6 | 11 | 14 |
| 5th week ... | 0 | 1 | 3 | 1 | 0 | 2 | 7 | 8 |
| 6th week ... | 0 | 0 | 2 | 0 | 0 | 2 | 2 | 10 |
| *Total to 21st Oct'r.* | *1* | *4* | *19* | *13* | *2* | *28* | *52* | *81* |

A slight epidemic of Influenza occurred while this experiment was being carried on, and that probably accounts for so large a number of fever cases in which parasites were not found. But it is curious that the proportion among those who were not taking quinine was so much greater than among those who were taking quinine.

If we consider the effect of the prophylactic dose of quinine on each class of fever we find among the quinine group one Quartan, but this case was one in which Quartan parasites had been present for many months, and he had a slight attack of influenza which was probably the cause of the fever. There were two Quartan among those who were not receiving quinine.

*Benign Tertian.*—Of the four cases that occurred among the quinine group, two were admitted on the day after the first dose of quinine was given and one on the fourth day. After that, the Benign Tertian almost disappeared from the quinine group. From the non-quinine group there were 28 Benign Tertian cases admitted. A weekly dose of twenty grains would probably prevent nearly all admissions for Benign Tertian.

*Malignant Tertian and Quotidian.*—The numbers gradually decreased among the quinine group. There were nineteen altogether, and in the non-quinine group there were 52.

A further experiment is being made by keeping a number of men inside mosquito curtains from sun-down till day-break. Their blood was examined carefully on three days so as to ensure that none of them had already parasites in their blood. It was

necessary to reject 10 altogether out of about 46 on this account. It is now past the middle of October (21st), and the Malarial season is almost at an end. Up to the present time none of these who have been confined in the mosquito curtains have had fever.

## Conclusion.

Whatever doubts we may have in regard to the part that mosquitoes play in carrying Malarial fever germs, there are two facts which have been proved conclusively: first, that the growth of Malarial parasites can be checked by quinine, and second, that Malarial fevers can be almost entirely prevented by the use of mosquito curtains. We hope to continue our experiments with a view to determining what part the mosquitoes play; but for the present it is satisfactory to think that our knowledge of Malaria has progressed in recent years in a way that the most sanguine enthusiast could scarcely have dreamt of a few years ago. It would be rash to expect that the Native population will universally be benefitted in the immediate future by the new light which has been thrown on this question; but it is, we think, reasonable to hope that the numerous Europeans who are employed in this country will benefit enormously by the knowledge derived from recent researches. There is a large Jail population, and if Malarial fevers are checked among them, the result will be a great saving to Government, and a valuable lesson to the Native population generally.

Jenner's discovery of Vaccination and Lord Lister's discovery of the use of Antiseptics have conferred incalculable advantages on mankind, and there

is every reason now to hope that the recent discoveries regarding Malaria will confer an equal, if not a greater, boon on residents in Tropical and sub-Tropical climates. Whether the credit will be given to Laveran the discoverer of the parasite, or to Celli, Grassi, and the numerous other Italians who differentiated and described the various kinds of parasites, all must agree that there are two English names which in any treatise on the subject of Malaria deserve to be written in large letters—the one **MANSON** the other **ROSS**.

# INDEX.

# NAME INDEX.



Note—At page 44 *for* Kya Thoung *read* Ko Tha Aung.